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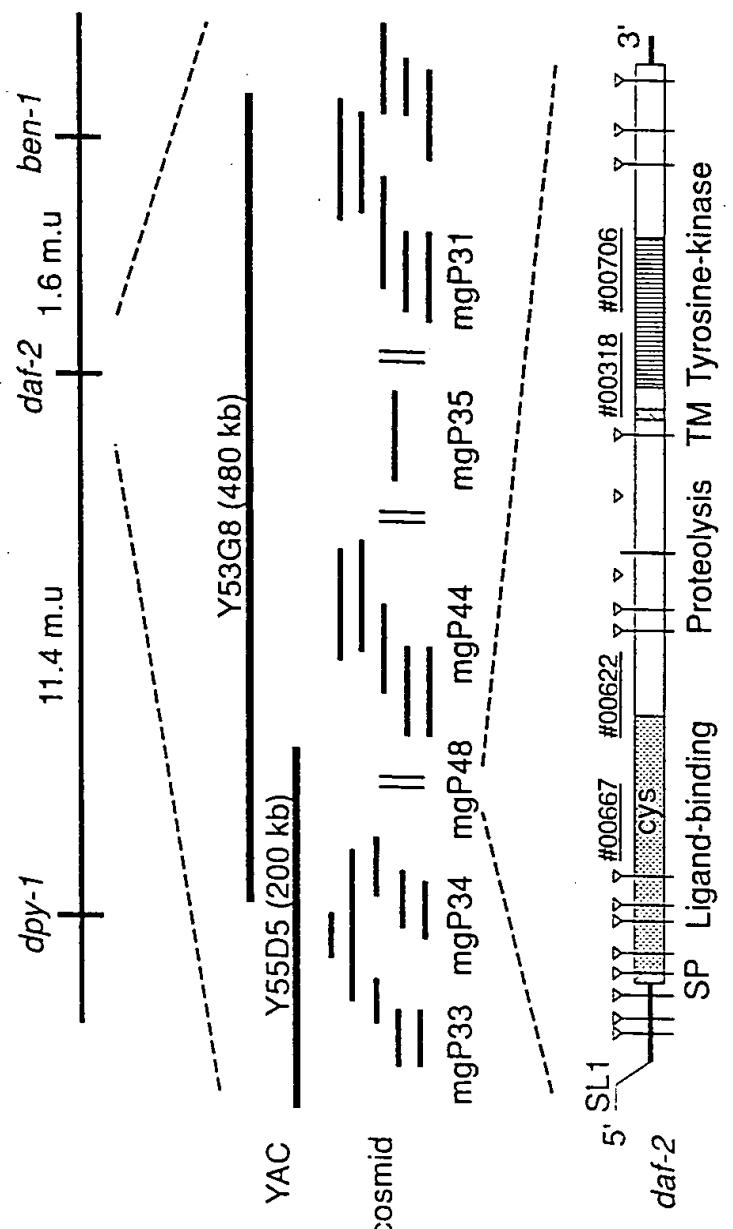


Fig. 1

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Fig. 2A

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Fig. 2B (sheet 2 of 3)

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Fig. 2B (sheet 3 of 3)

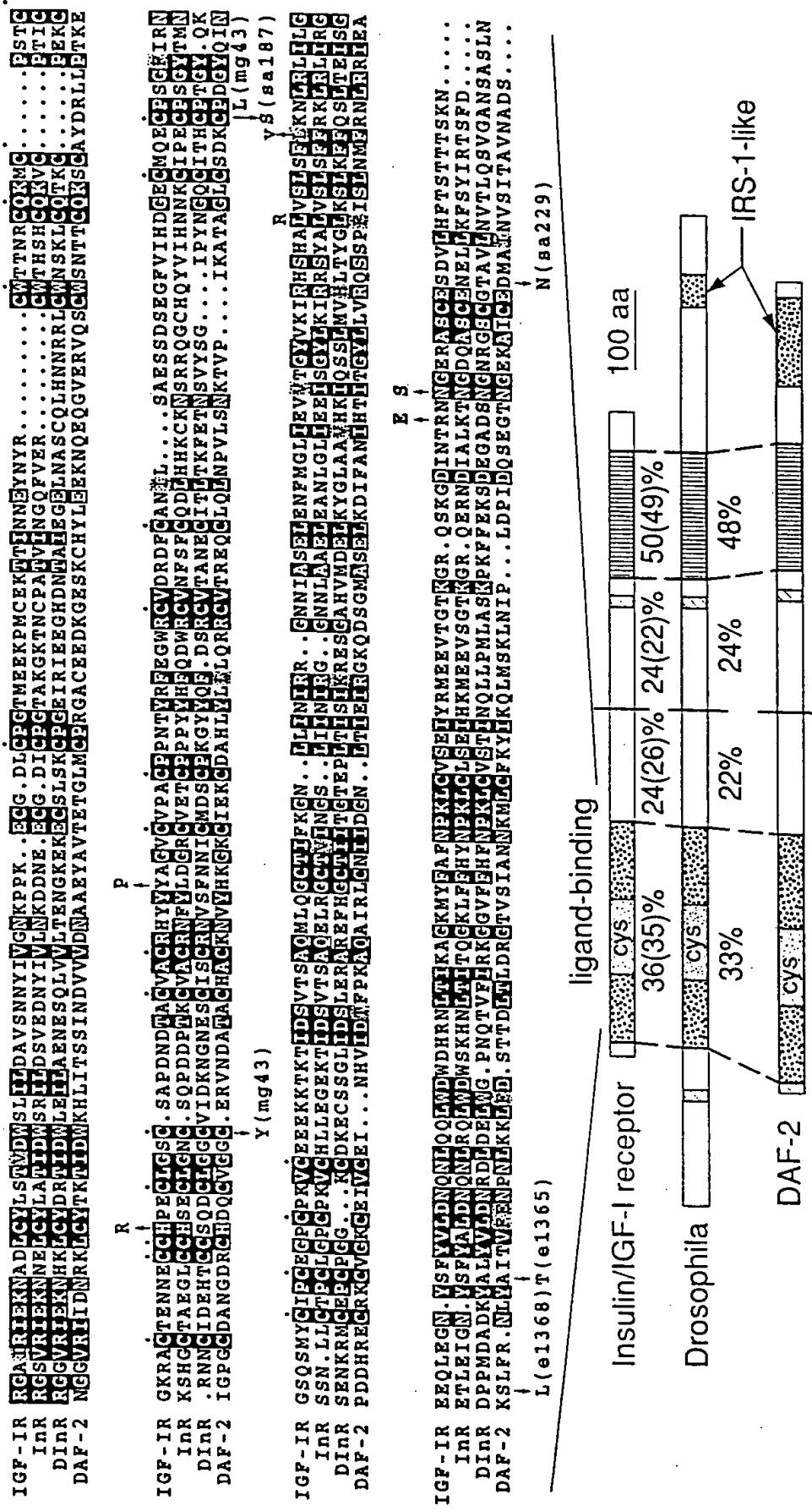
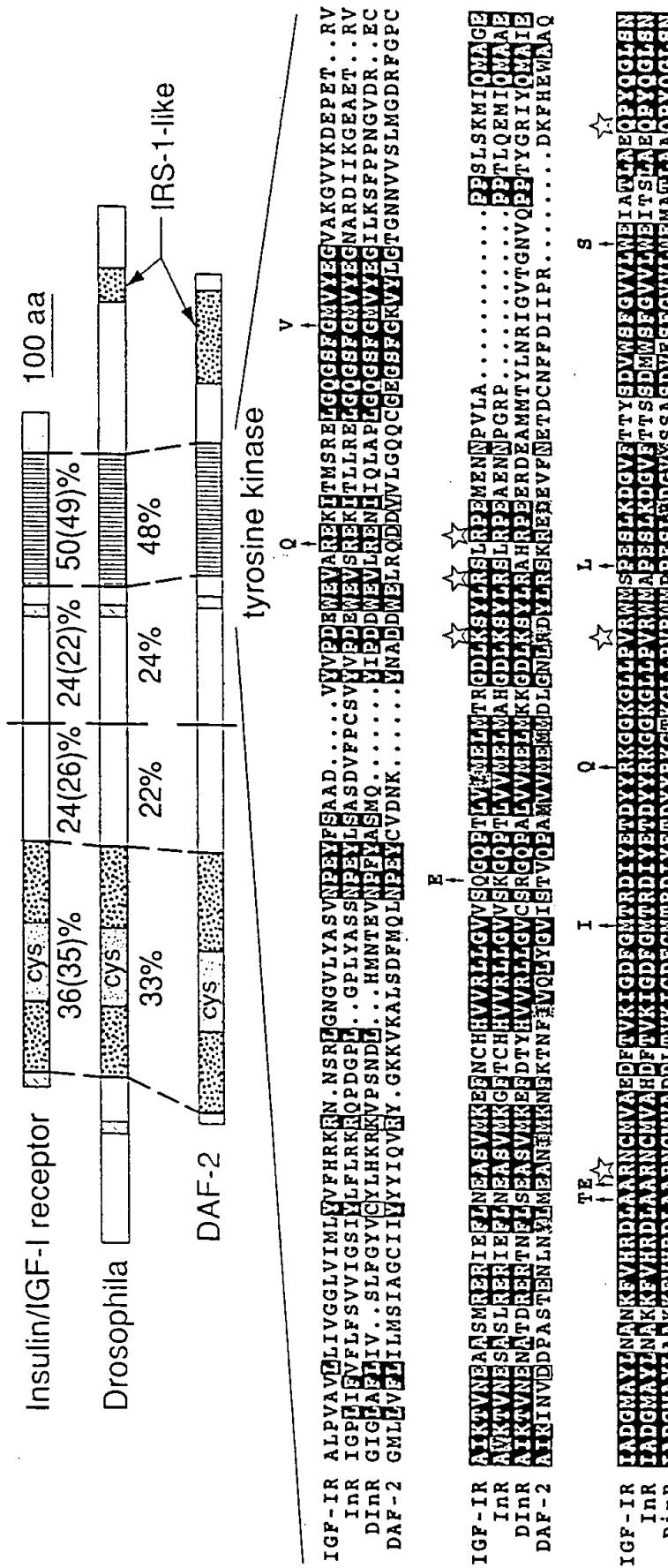


Fig. 2C (sheet 1 of 2)



111-2101

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EQVLFVY
EQVLFVY
EQVLFVY
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★
IGF-IR
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EQVLFVY
EQVLFVY
EQVLFVY
DINr
DAF-2
N-Baz19)
★
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Fig. 2C (sheet 2 of 2)

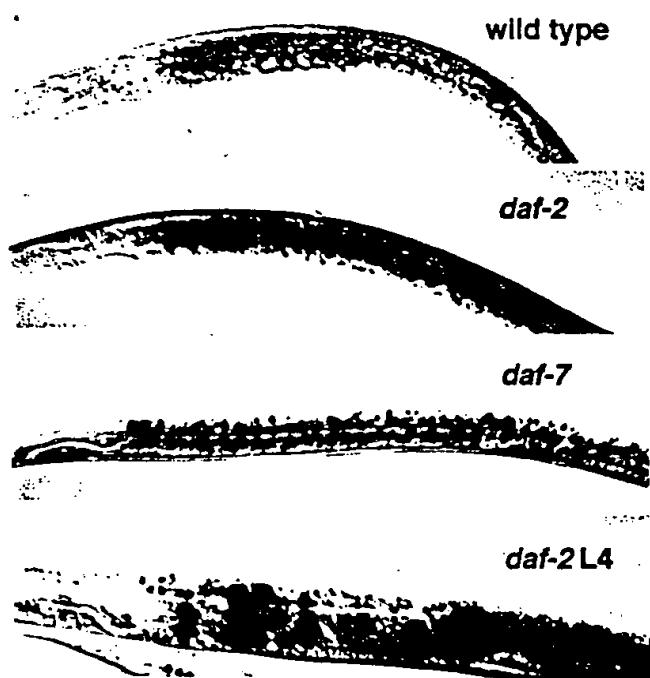


Fig. 3

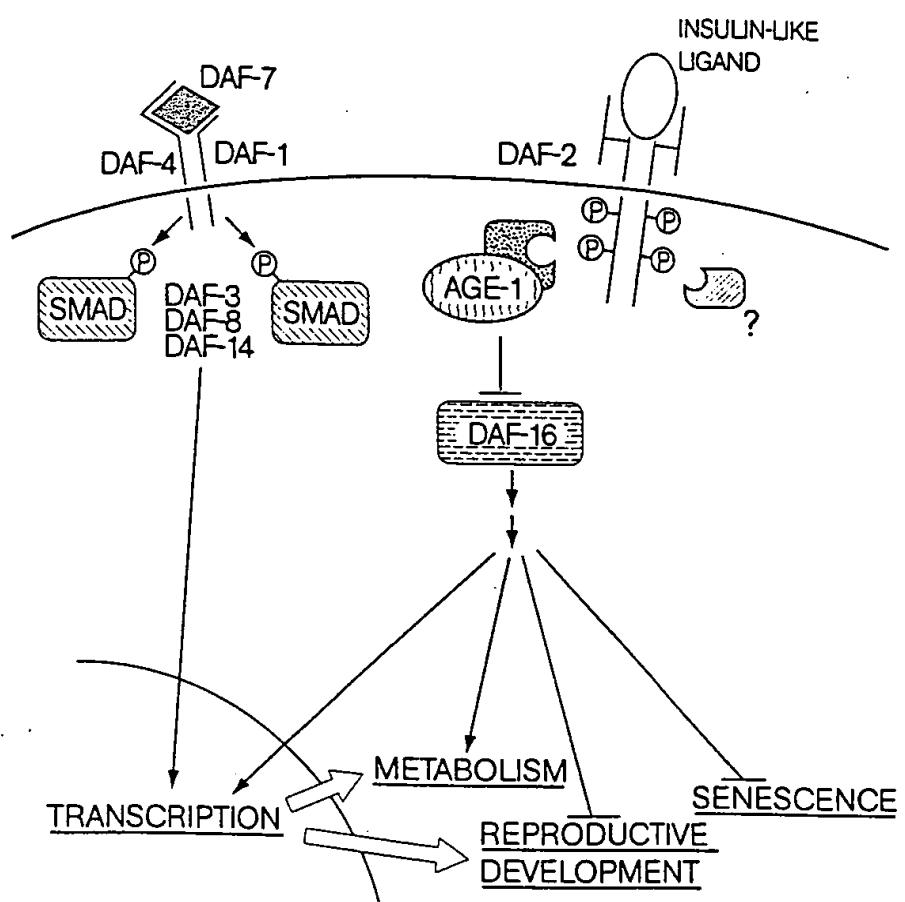


Fig. 4

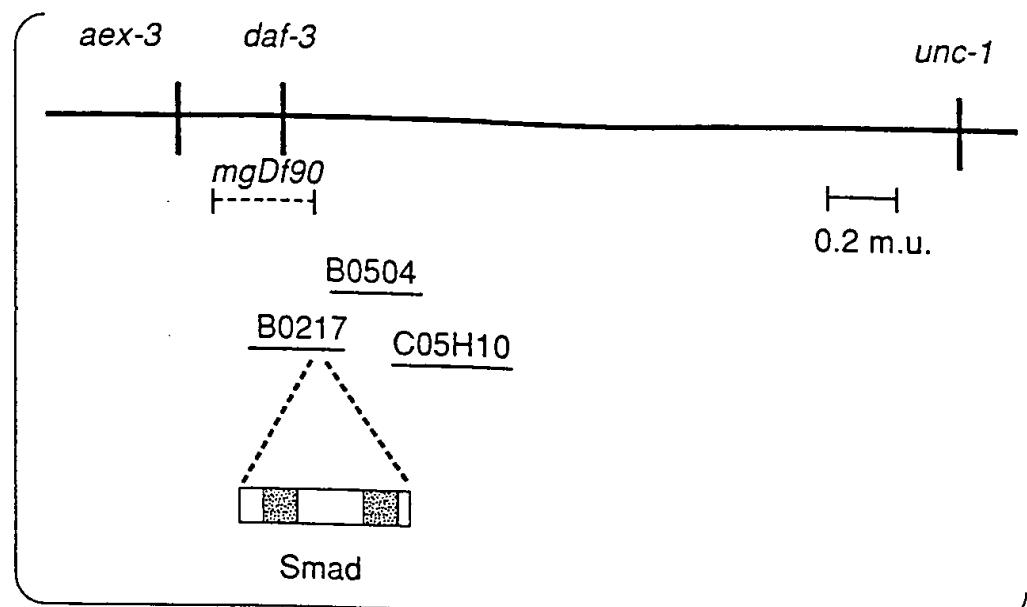


Fig. 5A

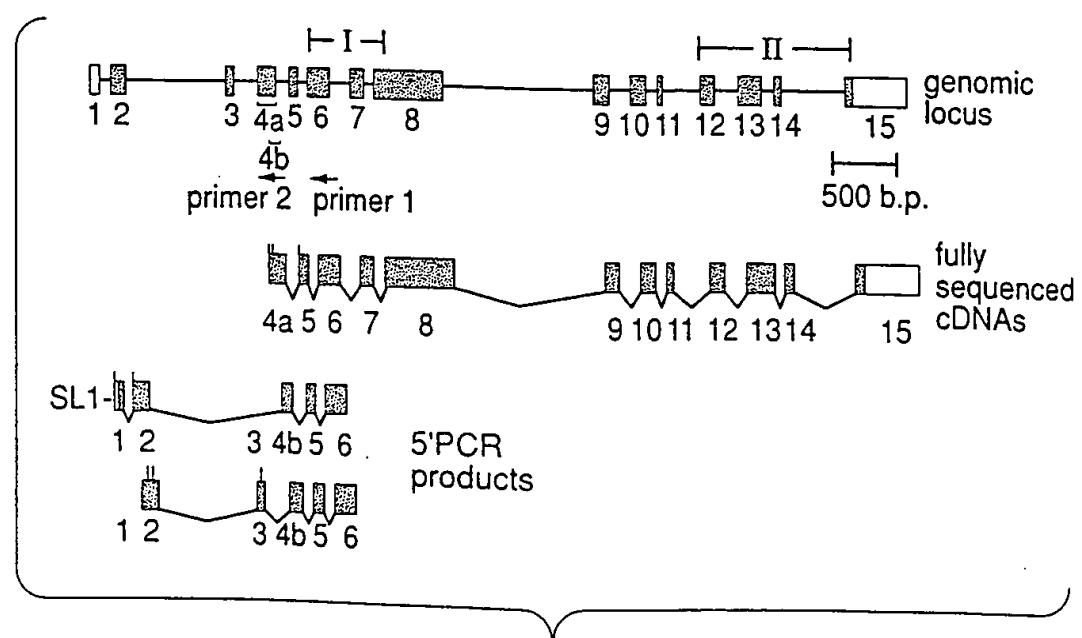


Fig. 5B

Domain I

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mg125 P->L

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Domain II

DAF-3	IVYYEKNLQIGE..KKCSRGNFHVDGGFI..CSENRYSLGLEPNPIREPVAFKV
DPC4	IAYFEMDVQVGETFKVPSSCPIVTVGDYVDPSSGDRFCLGQLSNVHRTEAIERA

mg132 G->E

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Fig. 5C

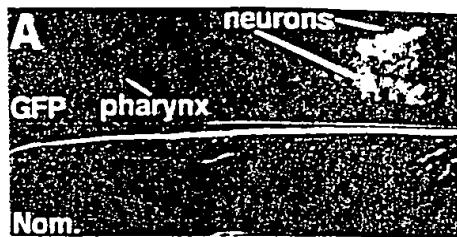


Fig. 6A

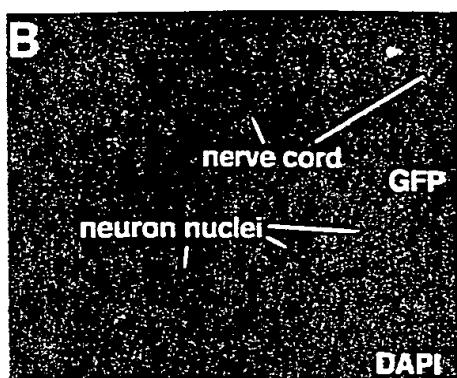


Fig. 6B

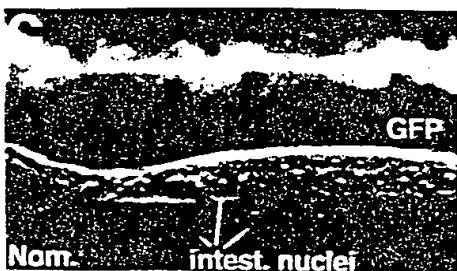


Fig. 6C

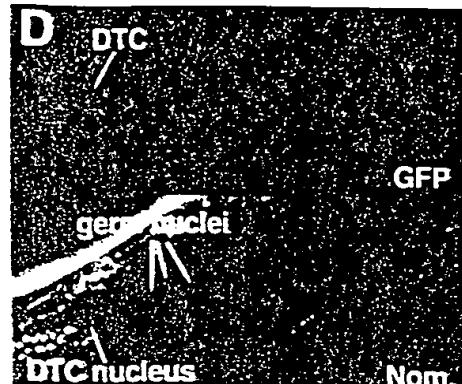


Fig. 6D



Fig. 6E



Fig. 6F



Fig. 6G

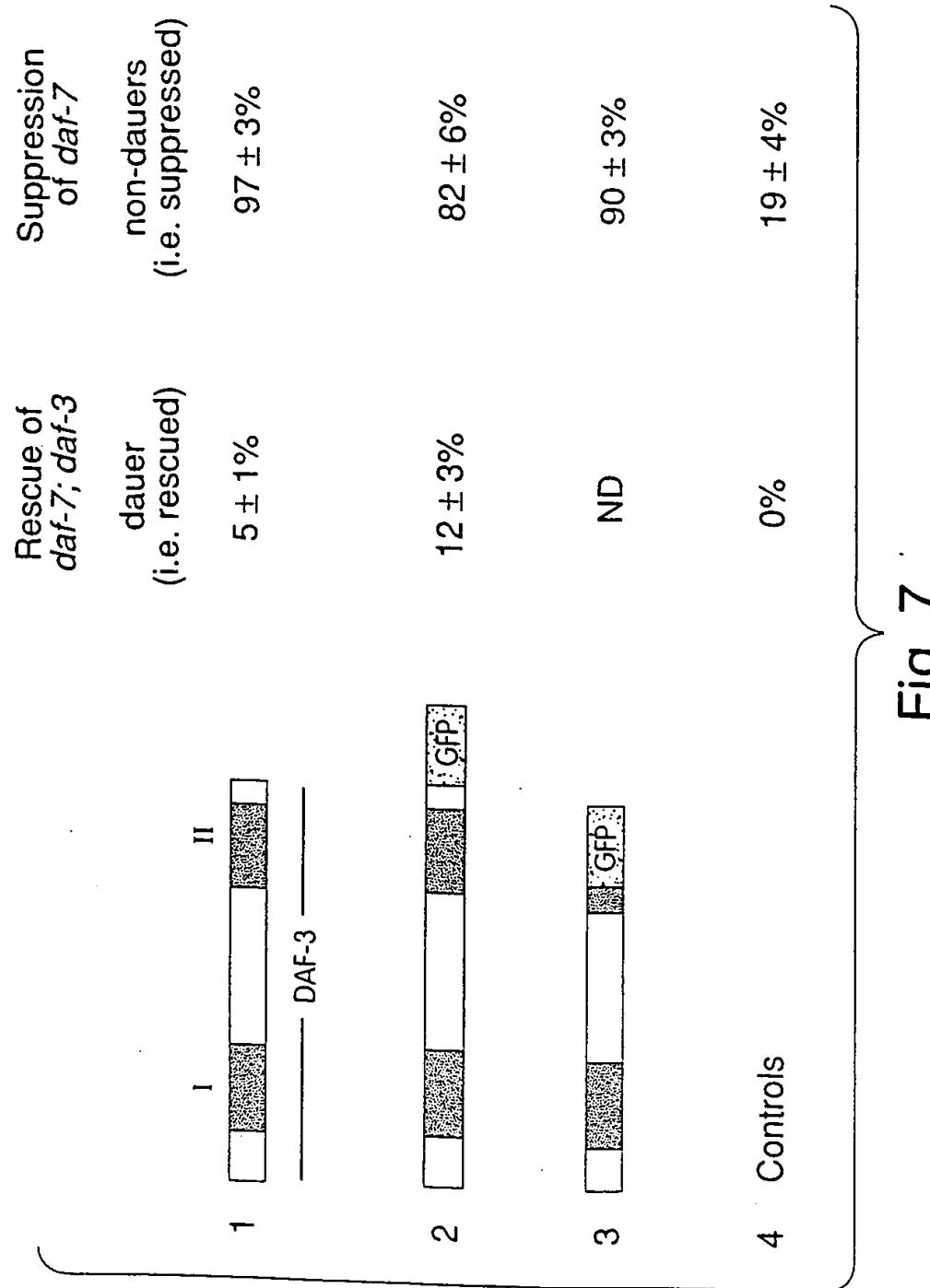




Fig. 8A

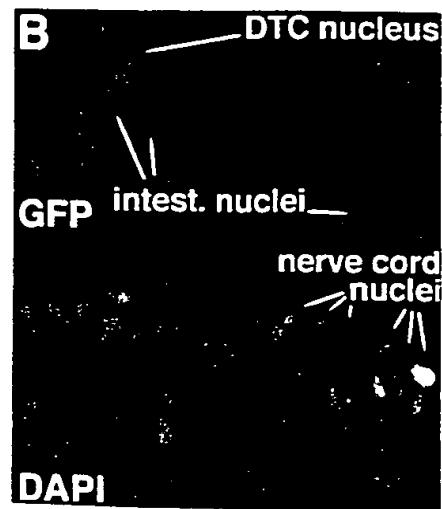
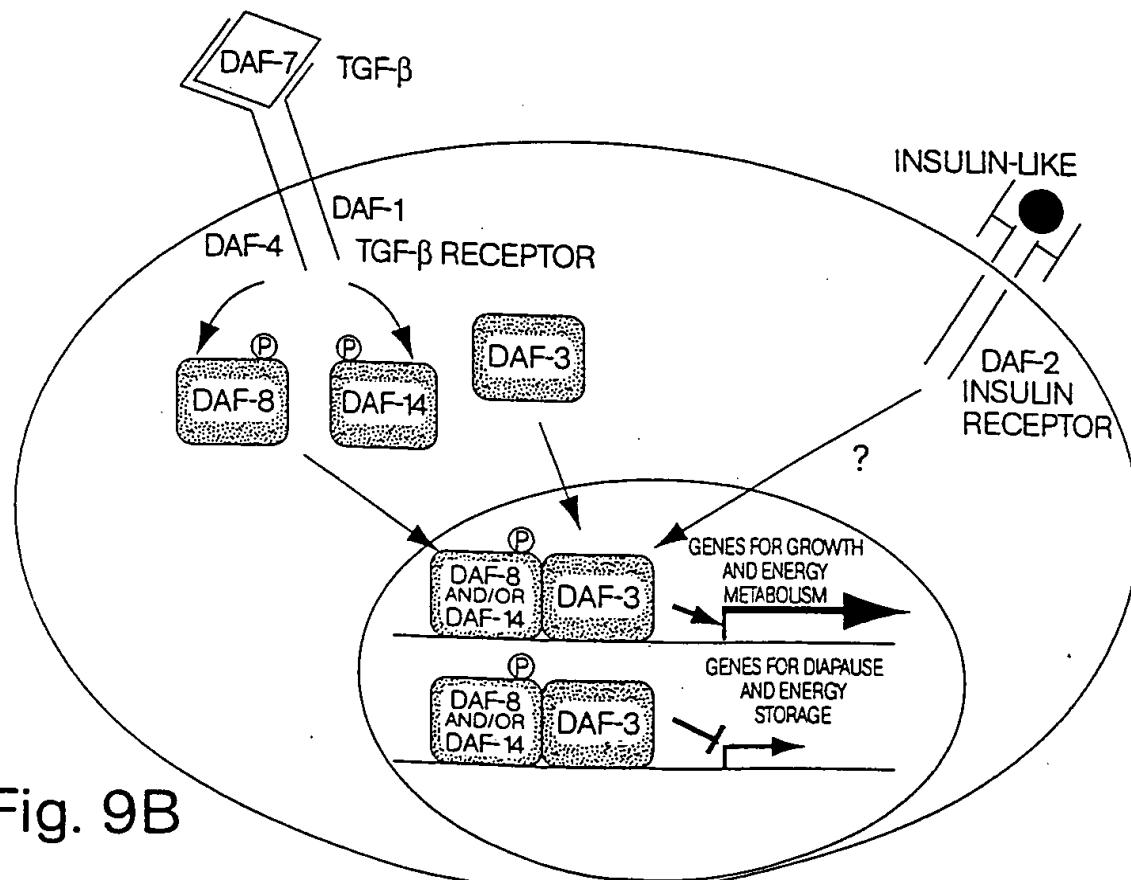
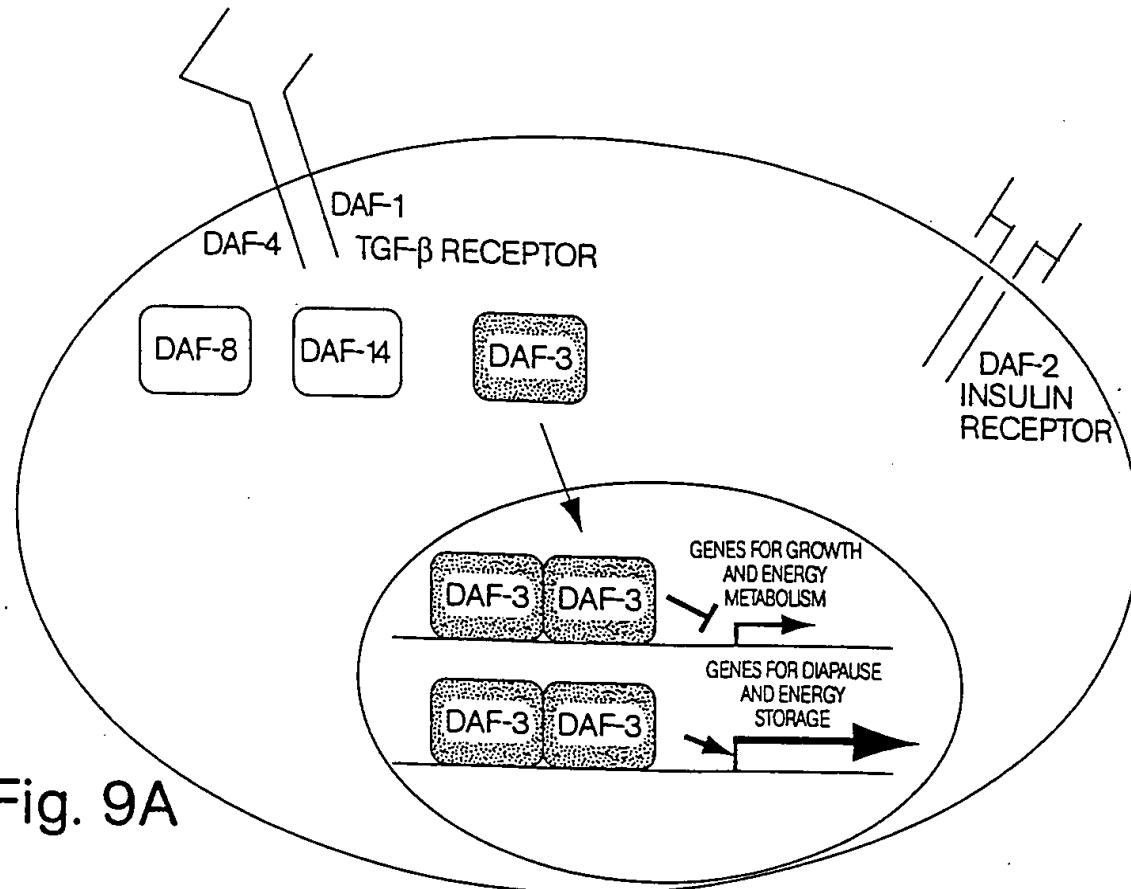
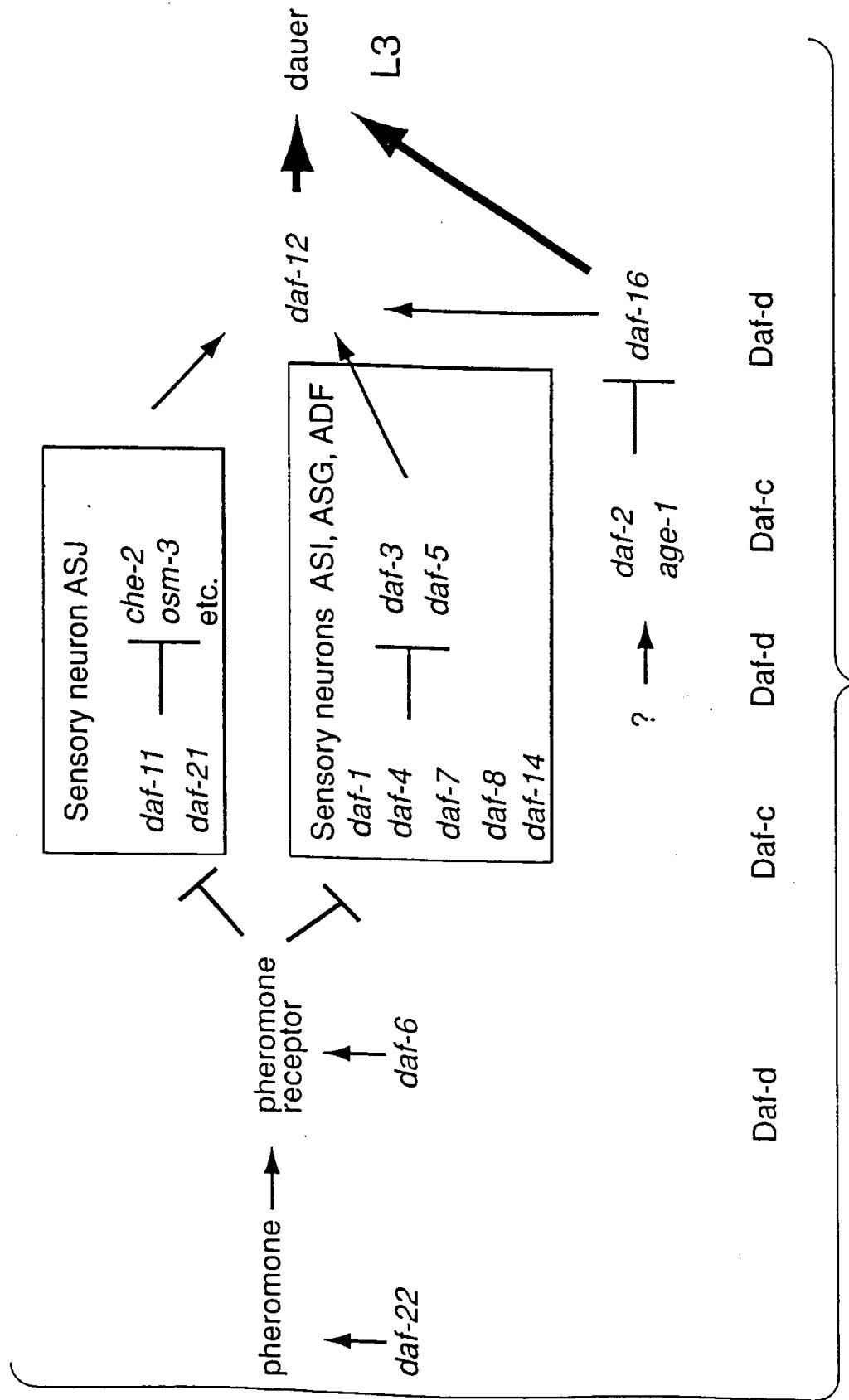


Fig. 8B





10
Fig.

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 1901 aaaaccgcat gaagtacccg gtatttgc tttctggta tctcgacgag
 1951 caatcaggag gcctaaagaa ggataaagtg cacaagttt acggatgtgc
 2001 gtctatcaa acgtttggtc tcaacgtttc caaacaatc atcagagacg
 2051 cgcttcttc caagcaaatg gcaacaatgt acttgcaagg aaaattgact

Fig. 11A (sheet 1 of 2)

2101 ccgatgaatt atatctacga gaagaagact caggaagagc tgcgaaggga
2151 agcaacacgc accactgatt cattggccaa gtactgttgc gtccgtgtct
2201 cgttctgcaa aggatttggc gaagcatacc cagaacgccc gtcaattcat
2251 gattgtccag tttggattga gttgaaaatc aacattgcct acgatttcat
2301 ggattcaatc tgccagttaca taaccaactg cttcgagccg ctaggaatgg
2351 aagattttgc aaaattggga atcaacgtca gtgatgacta aatgataact
2401 ttttcactc accctactag atactgatt agtcttattc caaatcatcc
2451 aacgatatac aacttttcc tttgaacttt gcatactatg ttatcacaag
2501 ttccaagcag tttcaataca aacataggat atgttaacaa cttttgataa
2551 gaatcaagtt accaactgtt cattgtgagc tttgagctgt atagaaggac
2601 aatgtatccc atacctcaat cttaatagt catcagtcac tggccccgca
2651 ccaattttt cgattcgcat atgtcatata ttgcaccgtg gcccctttta
2701 ttgttaacttt taatataattt tcttcccaac ttgtgaatat gattgatgaa
2751 ccaccatttt gagtaataaa tgtatTTT gtgg

Fig. 11A (sheet 2 of 2)

1 gtaatcaaat tgtaaaggaa aaatattaat agtcagagta cacataaatg
 51 ggtgatcatc ataatttaac gggccttccc ggtacctcca tcccgccaca
 101 gttcaactat tctcagcccg gtaccagcac cgaggcccgg ctttatggtg
 151 gaaaaccttc tcatggattg gaagatattc ctgatgtaga ggaatatgag
 201 aggaacctgc tcggggctgg agcaggtttt aatctgctca atgttaggaaa
 251 tatggctaattt gttcccacg agcacacaccc gatgatgtca ccagtgaata
 301 caactacaaa gattctacaa cgagggtttaaaaatgga aatcccggca
 351 tatttggatc cagacagtca ggatgtatc acggaaatgt gtgtcaacta
 401 cccggatcca gatttattt acacaaaaaaa cacaaatatg accgagtagc
 451 atttggatgt gttgaagctt ggaaaaccag cagtagatga agcacggaaa
 501 aagatcgaag ttcccacgc tagtgcggc ccaaacaaaaa ttgtagaata
 551 tttgatgtat tatagaacgt taaaagaaaag tgaactcata caactgaatg
 601 cgtatcgac aaaacgaaat cgattatcgt tgaacttggg caaaaacaat
 651 attgatcgag agttcgacca aaaagcttc gaggccctgg tgaaaaaatt
 701 gaaggataag aagaatgtc tccagaaccc gattgatgtg gttcttcaa
 751 aaggtaaaaa atataccgt tgcattacaa ttccaaggac acttgatggc
 801 cggttacagg tccacggaaag aaaaggttc cctcacgtag tctatggcaa
 851 actgtggagg tttatgaaa tgacaaaaaaa cgaaacgcgt catgtggacc
 901 actgcaagca cgcatttggaa ataaaaatg acatggatg cgtaatccc
 951 tatcactacg aaattgtcat tggaaactatg attgttggc agaggatca
 1001 tgacaatcga gatatgccgc cgccacatca acgctaccac actccaggc
 1051 ggcaggatcc agttgacgat atgagtagat ttataccacc agcttccatt
 1101 cgtccgcctc cgatgaacat gcacacaagg cctcagccta tgcctcaaca
 1151 attgccttca gttggcgaa cgtttggccca tcctctccca catcaggcgc
 1201 cacataaccc aggggttca catccgtact ccattgctcc acagacccat
 1251 taccctgttga acatgaaccc aattccgcaa atgcccggaaa tgccacaaat
 1301 gccaccaccc ctccatcagg gatatggaaat gaatggccg agttgtctt
 1351 cagaaaaacaa caatccattc cacaaaaatc accattataa tgatattagc
 1401 catccaaatc actattccta cgactgtggt ccgaacttgc acgggtttcc
 1451 aactccttat ccggattttc accatcctt caatcagcaa ccacaccgc
 1501 cgccacaact atcacaaaaac catacgccc aacaaggcag tcataacca
 1551 gggcaccaag gtcaggtacc gaatgtatcca ccaatttcaa gaccagtgtt
 1601 acaaccatca acagtccact tggacgtgtt ccgtcggtac tgtagacaga
 1651 catttggaaa tcgattttt gaaggagaaa gtgaacaatc cggcgcaata
 1701 attcggtcta gtaacaaatt cattgaagaa tttgattcgc cgatttgcgg
 1751 tgtgacagtt gttcgaccgc ggatgacaga cggtgaggtt ttggagaaca
 1801 tcatgcccga agatgcacca tattcatgaca tttgcaagt cattttgagg
 1851 ctcacatcag aaagtgtaac tttctcagga gagggggccag aagtttagtga
 1901 tttgaacgaa aaatggggaa caattgtgtt ctatgagaaa aatttgcaaa
 1951 ttggcgagaa aaaatgttcg agaggaaatt tccacgtgga tggcgattc
 2001 atttgctctg agaatcgtt a cagtctcgaa cttgagccaa atccaattag
 2051 agaaccagtg gcgtttaaag ttcgtaaagc aatagtggat ggaattcgct

Fig. 11B (sheet 1 of 2)

2101 tttcctacaa aaaagacggg agtgttggc ttcaaaaccg catgaagtac
2151 ccggtatgg tcacttctgg gtatctcgac gagcaatcag gaggcctaaa
2201 gaaggataaa gtgcacaaaag tttacggatg tgcgtctatc aaaacgtttg
2251 gcttcaacgt ttccaaacaa atcatcagag acgcgcttct ttccaagcaa
2301 atggcaacaa tgtacttgca agaaaaattt actccgatga attatatcta
2351 cgagaagaag actcaggaag agctgcgaag ggaagcaaca cgaccactg
2401 attcattggc caagtactgt tgtgtccgtg tctcggttcaaaaggattt
2451 ggagaagcat acccagaacg cccgtcaatt catgattgtc cagtttggat
2501 tgagttgaaa atcaacatgg cctacgattt catggattca atctgccagt
2551 acataaccaa ctgcttcgag ccgcgttggaa tggaagattt tgcaaaattt
2601 ggaatcaacg tcagtgtatca ctaaatgata actttttca ctcaccctac
2651 tagatactga ttttgtctta ttccaaatca tccaaacgata tcaaactttt
2701 tccttgaac tttgcataact atgttatac aagttccaag cagtttcaat
2751 acaaacatag gatatgttaa caacttttga taagaatcaa gttaccaact
2801 gttcattgtg agctttgagc tgtatagaag gacaatgtat cccatacctc
2851 aatcttaat agtcatcagt cactggtccc gcaccaattt tttcgattcg
2901 catatgtcat atattgcacc gtggcccttt ttattgtaac tttaatata
2951 ttttcttccc aacttgtgaa tatgattgat gaaccaccat tttgagtaat
3001 aaatgtatgg tttgtgg

Fig. 11B (sheet 2 of 2)

1 gtaatcaa at taaaaggaa aaatatta at agtcagagta cacataa atg
 51 ggtgatcatc ataatttaac gggccttccc ggtacctcca tcccgccaca
 101 gttcaactat tctcagcccg gtaccagcac cggaggcccg ctatggtg
 151 gaaaaccttc tcatggattt gaagatattc ctgatgtaga ggaatatgag
 201 aggaacctgc tcggggctgg agcagggttt aatctgctca atgttaggaaa
 251 tatggcta at gaatttaa ac caataatcac attggacacg aaaccaccc
 301 gtgatgccaa caagtcatc gcattcaatg gcgggtt gaa gctaattact
 351 ccgaaaactg aagttcccgaa cgagcacaca ccgatgtgt caccagt gaa
 401 tacaactaca aagattctac aacggagtgg tattaaaatg gaaatcccgc
 451 catattt gga tccagacagt caggatgtg accccggaaga tgggtgtcaac
 501 taccggatc cagatttatt tgacaca aacacaaa aacacaaaata tgaccgagta
 551 cgatttggat gtgttgaagc ttggaaaacc agcagtagat gaagcacgga
 601 aaaagatcga agttcccgac gctagtgcgc cgccaaacaa aattgttagaa
 651 tattt gatgtt attatagaac gttaaaagaa agtgaactca tacaactgaa
 701 tgcgtatcg g acaaaacgaa atcgattatc gttgaactt g tcaaaaaca
 751 atattgatcg agagttcgac caaaaagctt gcgagtccct ggtgaaaaaaa
 801 ttgaaggata agaagaatga tctccagaac ctgattgtg tggttctt
 851 aaaaggta ca aatataccg gttgcattac aattccaagg acactt gatg
 901 gccgg taca ggtccacgga agaaaagg tccctcacgt agtctatggc
 951 aaactgtgga ggttaatga aatgacaaa aacgaaacgc gtcatgtgga
 1001 ccactgcaag cacgcattt g aatgaaaag tgacatggta tgcgtgaatc
 1051 cctatcacta cgaaattt gtc attt gacta tgattgtt ggcagaggat
 1101 catgacaatc gagatatg cccgcacat caacgctacc acactccagg
 1151 tcggcaggat ccagttgacg atatgactg tagtatacca ccagcttcca
 1201 ttcgtccgccc tccgatgaa ac atgcacacaa ggcctcagcc tatgcctcaa
 1251 caattgcctt cagttggcgc aacgtttgc ccatcttcc cacatcaggc
 1301 gcccacataac ccagggttt cacatccgta ctccattgct ccacagaccc
 1351 attaccggtt gaacatgaa ac ccaattccgc aaatgccc aatgccacaa
 1401 atgcccaccac ctctccatca gggatatgga atgaatggc cgagttgctc
 1451 ttcagaaaac aacaatccat tccaccaaaa tcaccattat aatgatatta
 1501 gccatccaaa tcactattcc tacgactgtg gtccgaactt gtacgggtt
 1551 ccaactcctt atccggattt tcaccatcc ttcaatcagc aaccacacca
 1601 gccgcccacaa ctatcacaaa accatacg tc cacaaggc agtcatcaac
 1651 caggccacca aggtcaggta ccgaatgatc caccaattt aagaccagt
 1701 ttacaaccat caacagtca cttggacgtg ttccgtcggt actgtagaca
 1751 gacattt gga aatcgattt ttgaaggaga aagtgaacaa tccggcgc
 1801 taattcggtc tagtaacaaa ttcattgaa g aattt gattt gccgattt
 1851 ggtgtgacag ttgttcgacc g cggatgaca gacggtgagg tttggagaa
 1901 catcatgccc gaaatgocac catatcatga catttgc aag ttcattt
 1951 ggctcacatc agaaatgtta actttctca g gaggggcc agaagtt
 2001 gatttgaacg aaaaatggg aacaattgtg tactatgaga aaaatttgc
 2051 aattggcgag aaaaatgtt cgagaggaaa tttccacgtg gatggcggat

2101 tcatttgctc tgagaatcgt tacagtctcg gacttgagcc aaatccaatt
2151 agagaaccag tggcgtaaa agttcgtaaa gcaatagtgg atgaaattcg
2201 ctttcctac aaaaaagacg ggagtgttg gcttcaaaac cgcatgaagt
2251 acccggtatt tgtcacttct gggtatctcg acgagcaatc aggaggccta
2301 aagaaggata aagtgcacaa agtttacgga tgtcggtcta tcaaaacgtt
2351 tggcttcaac gtttccaaac aaatcatcag agacgcgcgtt cttccaaagc
2401 aaatggcaac aatgtacttg caaggaaaaat tgactccgat gaattatatac
2451 tacgagaaga agactcagga agagctgcga aggaaagcaa cacgcaccac
2501 tgattcattg gccaagttact gttgtgtccg tgcgtcgat tgcaaaggat
2551 ttggagaagc atacccagaa cggccgtcaa ttcatgattt tccagtttg
2601 attgagttga aaatcaacat tgcctacat ttcatggatt caatctgc
2651 gtacataacc aactgcttcg agccgctagg aatggaagat tttgc
2701 tggaaatcaa cgtcagtgtat gactaaatga taactttttt cactcaccct
2751 actagataact gatttagtct tattccaaat catccaacga tatcaaactt
2801 tttccttga actttgcata ctatgttac acaagttcca agcagttca
2851 atacaacat aggatatgtt aacaactttt gataagaatc aagttaccaa
2901 ctgttcattg tgagcttga gctgtataga aggacaatgt atccca
2951 tcaatctta atagtcata gtcactggcgc ccgcaccaat ttttcgatt
3001 cgccatgtc atatattgca ccgtggccct ttttattgtt acttttaata
3051 tattttcttc ccaacttgc aatatgattt atgaaccacc attttgagta
3101 ataaaatgtat tttttgtgg

Fig. 11C (sheet 2 of 2)

1 MKLIATSLV PDEHTPMMS P VNTTTKILQR SGIKMEIPPY LDPDSQDDDP
 51 EDGVNYPDPD LFDTKNTNMT EYDLDVLKLG KPAVDEARKK IEVPDASAPP
 101 NKIVEYLMYY RTLKESELIQ LNAYRTKRN R LSLNLVKNNI DREFDQKACE
 151 SLVKKLKD KK NDLQNLIDVV LSKGTKYTGC ITIPRTLDGR LQVHGRKGFP
 201 HVVYGKLWRF NEMTKNETRH VDHCKHAFEM KSDMVCVNPY HYEIVIGTMI
 251 VGQRDHDNRD MPPPHQRYHT PGRQDPVDDM SRFIPPASIR PPPMNMHTRP
 301 QPMPQQLPSV GATFAHPLPH QAPHNPGVSH PYSIAPQTHY PLNMNPPIQM
 351 PQMPQMPPL HQGYGMNGPS CSSENNNPFH QNHHYNDISH PNHYSYDCGP
 401 NLYGFPTPYP DFHHPFNQQP HQPPQLSQNH TSQQGSHQPG HQGQVPNDPP
 451 ISRPVLQPST VTLDVFRRYC RQTFGNRFFE GESEQSGAII RSSNKFIEEF
 501 DSPICGTVV RPRMTDGEVL ENIMPEDAPY HDICKFILRL TSESVTFSGE
 551 GPEVSDLNEK WGTIVYYEKN LQIGEKKCSR GNFHVDGGFI CSENRYSLGL
 601 EPNPIREPVA FKVRKAIVDG IRFSYKKDGS VWLQNRMKYP VFVTSGYLDE
 651 QSGGLKKDKV HKVYGCASIK TFGFNVSKQI IRDALLSKQM ATMYLQGKLT
 701 PMNYIYEKKT QEELRREATR TTDSSLAKYCC VRVSFCKGFG EAYPERPSIH
 751 DCPVWIELKI NIAYDFMDSI CQYITNCFEP LGMEDFAKLG INVSD

Fig. 12A

1 MGDHHNLTGL PGTSIPPQFN YSQPGTSTGG PLYGGKPSHG LEDIPDVEEY
51 ERNLLGAGAG FNLLNVGNMA NVPDEHTPMM SPVNTTTKIL QRSGIKMEIP
101 PYLDPDSQDD DPEDGVNYPD PDLFDTKNTN MTEYDLDVLK LGKPAVDEAR
151 KKIEVPDASA PPNKIVEYLM YYRTLKESEL IQLNAYRTKR NRLSLNLVKN
201 NIDREFDQKA CESLVKKLKD KKNDLQLNID VVLSKGTKYT GCITIPRTLD
251 GRLQVHGRKG FPHVVYGKLW RFNEMTKNET RHVDHCKHAF EMKSDMVCVN
301 PYHYEIVIGT MIVGQRDHDN RDMPPPHQRY HTPGRQDPVD DMSRFIPAS
351 IRPPPMNMHT RPQPMPPQQLP SVGATFAHPL PHQAPHNPGV SHPYSIAPQT
401 HYPLNMNPIP QMPQMPQMPP PLHQGYGMNG PSCSSENNNP FHQNHHYNDI
451 SHPNHYSYDC GPNLYGFPTP YPDFHHPFNQ QPHQPPQLSQ NHTSQQGSHQ
501 PGHQGQVPND PPISRPVLQP STVTLDVFRR YCRQTFGNRF FEGESEQSGA
551 IIRSSNKFIE EFDSPICGVT VVRPRMTDGE VLENIMPEDA PYHDICKFIL
601 RLTSESVTFS GEGPEVSDLN EKWTGIVYYE KNLQIGEKKC SRGNFHVDGG
651 FICSENRYSL GLEPNPIREP VAFKVRKAIV DGIRFSYKKD GSVWLQNRMK
701 YPVFVTSGYL DEQSGGLKKD KVHKVYGCAS IKTFGFNVSK QIIRDALLSK
751 QMATMYLQGK LTPMNYIYEK KTQEELRREA TRTTDSLAKY CCVRVSFCKG
801 FGEAYPERPS IHDCPVWIEL KINIAYDFMD SICQYITNCF EPLGMEDFAK
851 LGINVSDD

Fig. 12B

1 MGDHHNLTGL PGTSIPPQFN YSQPGTSTGG PLYGGKPSHG LEDIPDVEEY
 51 ERNLLGAGAG FNLLNVGNMA NEFKPIITLD TKPPRDANKS LAFNGGLKLI
 101 TPKTEVPDEH TPMMSPVNNT TKILQRSGIK MEIPPYLDPD SQDDDPEDGV
 151 NYPDPDLFDT KNTNMTEYDL DVLKLGKPAV DEARKKIEVP DASAPPNKIV
 201 EYLMYYRTLK ESELIQLNAY RTKRNRLSLN LVKNNIDREF DQKACESLVK
 251 KLKDKKNDLQ NLIDVVLSKG TKYTGCITIP RTLDGRLQVH GRKGFPHVYY
 301 GKLWRFNEMT KNETRHVDHC KHADEMKSMD VCVNPYHYEI VIGTMIVGQR
 351 DHDNRDMPPP HQRYHTPGRQ DPVDDMSRFI PPASIRPPP NMHTRPQPMP
 401 QQLPSVGATF AHPLPHQAPH NPGVSHPYSI APQTHYPLNM NPIPQMPQMP
 451 QMPPPLHQGY GMNGPSCSSE NNNPFHQNH YNDISHPNHY SYDCGPNLYG
 501 FPTPYPDFHH PFNQQPHQPP QLSQNHTSQQ GSHQPGHQGQ VPNDPPISRP
 551 VLQPSTVTLD VFRRYCRQTF GNRFFESE QSGAIIRSSN KFIEFDSP
 601 CGVTVVRPRM TDGEVLENIM PEDAPYHDIC KFILRLTSES VTFSGEGPEV
 651 SDLNEKWGTI VYYEKNLQIG EKKCSRGNFH VDGGFICSEN RYSLGLEPNP
 701 IREPVAFKVR KAIVDGIRFS YKKDGSVWLQ NRMKYPVFVT SGYLDEQSGG
 751 LKKDKVHKVY GCASIKTFGF NVSKQIIRDA LLSKQMATMY LQGKLTPMNY
 801 IYEKKTQEEL RREATRTTDS LAKYCCVRVS FCKGFGEAYP ERPSIHDCPV
 851 WIELKINIAY DFMDSCICQYI TNCFEPLGME DFAKLGINV DD

Fig. 12C

09876543210

tgcattttcaagccgaagcaatcaagaccaaagccaatcaacttactcacttttttccagaacccaaactttttgtgt
 tcaactttcccaaaaaccgttcaagctgctgccttactctcatccctccttactccttcttctgtccgctacta
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cagaatgaaggagccgaaagagactcggtggatttaatccagatgaaagccaggaatgatccacggcgtacacg
tgaacgatccaataactattgagacgactacaaggctcaactcgaaaaatctcgccggagccaagaagaggataaagg
agagagcattgatggctcccttcaactcgacacttaatggaaattcgattgcccgtattcaacgatttctcacat
ttgtatgatgatgattcaatgcaaggagcattgataacgttccatcatttcgcccccgaactcaatcgaaaccttc
gattcctggatcgctcggtttctccagctattggagtgatctatgatgatctagaattccatcatgggttgc
gcaatcggttccagcaattcaagtgtatattgtttagataactgatcaatcgatcgactactcatattgg
ggagttcagattaagcaggagtcgaagccgattaagacggaaccaattgtccaccaccatcataccacgattgaaacag
tgtccgtggatcggtgtcagaatccacttccatcgaaatccattgtccagactacttcaagccaaatgcccactac
cggtgcctatggaaactatcaaaatggataactccatcaattggctatcaacatccactcatctccactgcct
ggaattcaatcggtggattttagtgcacagcatactgtcgcttccatcgcttccatcgatcgacttcaagccaaatg
gacacttcccgatcagccactgtgatggactatgtgatgttgcattgcataactgatgactgatcgacttcaagccaaatg
agcatattcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
ggagtggaaaatctccgtctcatcttcaatccctacccatcacacactcaacgatcatcagccagaccatcaat
attctccaaatttgcgtcgtaatttttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
ctttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
ccctaatcgaaaatcgaaaaaccgttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
tccaggttcttcaactcttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
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tcctcttttttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
gaatccctccgtatacacacacacatgatcactccaaatccatcttgcatttgcatttgcatttgcatttgcatttgc
tacaaaacattattgtctttgttatattgcaccacgtcgatccatcgatccatcgatccatcgatccatcgatcc
actttttctcgaaaaatttacaaacacacaaaaatccatcgatccatcgatccatcgatccatcgatccatcg
gatccatcgatccatcgatccatcgatccatcgatccatcgatccatcgatccatcgatccatcgatccatcg
gcttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
ttccaaattttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc
tcgttcctccctccgcccccaatataatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgcatttgc

Fig. 13B

MMEMLVDQGTDASSASTSTSSVSRFGADTFMNTPDDVMMNDMEPIPRDR
CNTWPMRRPQLEPPLNSSPIIHEQIPEEDADLYGSNEQCGQLGGASSNGST
AMLHTPDGSNSHQTSFPSDFRMSESPDDTVSGKTTTRRNAWGNMSYAE
TTAIMASPEKRLTLAQVYEWMVQNVPYFRDKGDSNSSAGWKN
SRFMRIQNEGAGKSSWWV
INPDAKPGMNPRRTRERSNTIETTTKAQLEKSR
RGAKKRRIKERALMGSLHSTLNGNSIAGSIQTISHDLYDDDSMQGAFDNVPS
SFRPRTQS
NL
SIPGSSSRVSPAIGSDIYDDLEF
PSWVGE
SVP
AIPSDIVDR
TDQMRIDATTHIGGVQIKQESKPIKTEPIAPPSY
HELNSVRGSCAQNPLL
RNPIV
PSTNF
KPMPLPGAY
GNYQNGG
ITPINWL
STSNS
SPLPGI
QSCG
I
VA
AQHTV
ASS
S
AL
PID
LEN
L
TLP
DQPL
MDT
MDV
DAL
IR
HELS
QAGG
OHI
F
DL

Fig. 14A

MQQYIYQESSATIPHHLNQHNNPYHPMHPHQQLPQPLLNLNMTT
LTSSGSSVASSIGGAQCSPCASGSSTAATNSSQQQQTVGQMLAASVPCSS
SGMTLGMSLNLSQGGGPMPAKKRCRKPTDQLAQKKPNPWGEESYSDIIA
KALE SAPDGRKLNEIYQWFSDNIPYFGERSSPEEAGWKNSIRHNLSLHS
RFMRIQNEGAGKSSWWVINPDAKPGMNRTRERSNTIETTKAQLEKSRR
GAKKRIKERALMGSLHSTLNGNSIAGSIQTISHDLYDDDSMQGAFDNVPSS
FRPRTQSNL SIPGSSSRVSPAIGSDIYDDLEFPSWVGESVPAIPSDIVDRT
DQMRIDATTHIGGVQIKQESKPIKTEPIAPPPSYHELNSVRGSCAQNPLLR
NPIVPSTNFKPMLPGAYGNYQNGGITPINWLSTSNSSPLPGIQSCGIVAA
QHTVASSSALPIDLENLTLPDQPLMDTMDVDALIRHELSOAGGOHIHFDL

Fig. 14B

1 cggaagccat ggagctcgag atctgattgc tggacacgga cggaactccg acgtatctcg
 61 cagatgcattt ttaacatttt acatccacaa ctgcaaacga tggtcgagca gtggcaatg
 121 cgagaacgcc catcgctgga gaccgagaat ggcaaaggat cgctgctcct ggaaaatgaa
 181 ggtgtcgag atatcatcac tatgtgtcca ttcggagaag ttattagtgt agtattccg
 241 tggtttctt caaatgtcg aacatcgta gaaatcaagc tatcagattt caaacatcaa
 301 ctttcgaat tgattgctcc gatgaagtgg ggaacatatt cctaaagcc acaggattat
 361 gtgttcagac agttgaataa ttccggcgaa attgaagtta tatttaacga cgatcaaccc
 421 ctgtcgaaat tagagctcca cggcactttc ccaatgctt ttctctacca acctgatgga
 481 ataaacaggg ataaagaatt aatgagtgtat aatagtattt gtctaggata ctcactggat
 541 aaactggaag agagcctcga tgaggaactc cgtcaatttc gtgcttctc ctgggctcgt
 601 acgaagaaaa cgtgcttgac acgtggactt gagggtacca gtcactacgc gttcccccga
 661 gaacagtact tgggtgttgg tgaatcgtgc cggaaagatt tggaaatcaaa agtcaaggct
 721 gccaagctga gttatcagat gtttggaga aaacgtaaag cgaaatcaa tggagttgc
 781 gagaaaaatga tgaagattca aattgaattt aatccgaacg aaactccgaa atctctgctt
 841 cacacgtttc tctacgaaat gcgaaaattt gatgtatacg ataccgatga tcctgcagat
 901 gaaggatggt ttcttcaatt ggctggacgt accacgtttt ttacaaatcc agatgtcaaa
 961 cttacgtctt atgatggtgt ccgttcggaa ctggaaagct atcgatgccc tggattcggt
 1021 gttcgccgac aatcactagt cctcaaagac tattgtcgcc caaaaccact ctacgaacca
 1081 cattatgtga gggcacacga acgaaaactt gctctagacg tgctcagcgt gtctatagat
 1141 agcacaccaa aacagagcaa gaacagtgc atggttatga ctgattttcg tccgacagct
 1201 tcactcaaac aagtttcaact ttgggacctt gacgcgaatc ttatgatacg gcctgtgaat
 1261 atttctggat tcgatttccc ggccgacgtg gatatgtacg ttcgaatcga attcagtgt
 1321 tatgtgggaa cactgacgct ggcacatcaaaa tctacaacaa aagtgaatgc tcaatttgca
 1381 aaatggaaata agggaaatgtt cacttttgc tatacatga aggatatgcc accatctgca
 1441 gtactcagca ttctgtttt gtacggaaaa gtgaaattaa aaagtgaaga attcgaagtt
 1501 ggtgggtaa atatgtccct aaccgattgg agagatgaac tacgacaagg acaatttttta
 1561 ttccatctgt gggctcctga accgactgcc aatcgttagta ggatcggaga aatggagca
 1621 aggataggca ccaacgcagc gttacaattt gaaatctcaa gttatgggtgg tagagttcga
 1681 atgccgagtc aaggacaata cacatatctc gtcaagcacc gaagtacttg gacggaaact
 1741 ttgaatattt tgggtgatga ctatgagtcg tttatcagag atccaggata taagaagctt
 1801 cagatgcttgc tcaagaagca tgaatctgga attgtatttag aggaagatga acaacgtcat
 1861 gtctggatgt ggaggagata cattcaaaa caggagcctg atttgcctcat tttgtctcc
 1921 gaactcgcat ttgtgtggac tgatcgtgag aactttccg agctctatgt gatgcttggaa
 1981 aaatggaaac cggcggatgt ggcagccgcg ttgactttgc ttggaaaacg ttgcacggat
 2041 cgtgtgattt gaaagttgc agtggagaag ttgaatgagg agctgagccc ggtcacattc
 2101 catctttca tattgcctct catacaggcg ttgaagtacg aaccgcgtgc tcaatcgaa
 2161 gttggaaatga tgctcttgc tagagctctc tgcgattatc gaattggaca tcgacttttcc
 2221 tggctgctcc gtgcagagat tgctcgatgg agagattgtt atctgaaaaat tgaagaatat
 2281 cggcgtatct cacttctgat ggaagcttac ctccgtggaa atgaagagca catcaagatc
 2341 atcacccgac aagttgacat gttgtatgag ctcacacgaa tcagcactct tttgtcaagga
 2401 atgccaatggaaatggaaactg atgttgcacgac gttgatcgat tagtcataaa
 2461 atggaaaata tggattctcc actggatcct gtgtacaaac tgggtgaaat gataatcgac
 2521 aaagccatcg tccttaggaag tgcaaaaacgt ccgttaatgc ttcactggaa gaacaaaaat
 2581 ccaaaagatgttgc acctgcaccc tccgttctgt gcaatgatct tcaagaatgg agacgatctt
 2641 cgccaggaca tgcttgcattc tcaagttctc gaagttatgg ataacatctg gaaggctgca

Fig. 15 (sheet 1 of 2)

2701 aacattgatt gctgttgaa cccgtacgca gttcttccaa tggagaaat gattggatt
2761 attgaagttg tgcctaattg taaaacaata ttcgagattc aagttgaaac aggattcatg
2821 aatacagcag ttccggatcat tgatccttcg tttatgaata agtggattcg gaaacaatgc
2881 ggaattgaag atgaaaagaa gaaaagcaaa aaggactcta cgaaaaatcc catcgaaaag
2941 aagattgata atactcaagc catgaagaaa tattttgaaa gtgtcgatcg attcctatac
3001 tcgtgtgtt gatattcagt tgccacgtac ataatggaa tcaaggatcg tcacagtat
3061 aatctgatgc tcactgaaga tggaaaatat gtccacattt atttcggtca cattttggg
3121 cacgaaaaga ccaaacttgg gatccagcga gatcgtaac cgtttattct aaccgaacac
3181 tttatgacag tgattcgatc gggtaaatct gtggatggaa attcgatga gctacaaaaa
3241 ttcaaaacgt tatcgatcgaa agcctacgaa gtaatgtgaa ataatcgaga tttgttcgtt
3301 tccttggta ccttgatgct cgaaatggag ttgcctgagc tgcgacgaa agcggatttg
3361 gatcatttga agaaaaaccct cttctgcaat ggagaaagca aagaagaagc gagaaagtt
3421 ttgcgtggaa tctacgaaga agccttcaat ggatcatggt ctacaaaaac gaattggctc
3481 ttccacgcag tcaaacacta ctga

Fig. 15 (sheet 2 of 2)

0 0 0 0 0 0 0 0 0 0

1 RKPWSSRSDC WTRTELRRIS QMHVNILHPQ LQTMVEQWQM RERPSLEHEN GKGSLLLNE
 61 GVADIITMCP FGEVISVVFP WLANVRTSL EIKLSDFKHQ LFELIAPMKW GTYSVKPQDY
 121 VFRQLNNFGE IEVIFNDDQP LSKLELHGTF PMLFLYQPDG INRDKELEMSD ISHCLGYSLD
 181 KLEESLDEEL RQFRASLWAR TKKTCLTRGL EGTSHYAFPE EQYLCVGESC PKDLESKVKA
 241 AKLSYQMFWR KRKAЕINGVC EKMMKIQIEF NPNETPKSLL HTFLYEMRKL DVYDTDDPAD
 301 EGWFLQLAGR TTFVTNPDVK LTSYDGVRSE LESYRCPGFV VRRQSLVLKD YCRPKPLYEP
 361 HYVRAHERKL ALDVLSVSID STPKQSKNSD MVMTDFRPTA SLKQVSLWDL DANLMIRPVN
 421 ISGFDFPADV DMYVRIEFSV YVGTLTLASK STTKVNAQFA KWNKEMYTFD LYMKDMPPSA
 481 VLSIRVLYGK VKLKSEEFEV GWVNMSLTDW RDELRQGQFL FHLWAPEPTA NRSRIGENGA
 541 RIGTNAAVTI EISSYGGRVR MPSQGQYTYL VKHRSTWTET LNIMGDDYES CIRDPGYKKL
 601 QMLVKKHESG IVLEEDEQRH VWMWRRYIQQ QEPDLLIVLS ELAFVWTDRE NFSELYVMLE
 661 KWKPPSVAAA LTLLGKRCTD RVIRKFAVEK LNEQLSPVTF HLFILPLIQA LKYEPRAQSE
 721 VGMMILLTRAL CDYRIGHRLF WLLRAEIARL RDCDLKSEEEY RRISLMEAY LRGNEEHIKI
 781 ITRQVDMVDE LTRISTLVKG MPKDVATMKL RDELRSISHK MENMDSPPLDP VYKLGEMIID
 841 KAIVLGSAKR PLMLHWKNKN PKSDLHLPFC AMIFKNGDDL RQDMLVLQVL EVMDNIWKA
 901 NIDCCLNPYA VLPMGEMIGI IEVVPNCKTI FEIQVGTGFM NTAVRSIDPS FMNKWIRKQC
 961 GIEDEKKKSK KDSTKNPIEK KIDNTQAMKK YFESVDRFLY SCVGYSVATY IMGIKDRHSD
 1021 NLMLTEDGKY VHIDFGHILG HGKTKLGIQR DRQPFILTEH FMTVIRSGKS VDGNSHELQK
 1081 FKTLCVEAYE VMWNNRDLFV SLFTLMLGME LPELSTKADL DHLKKTLFCN GESKEEARKE
 1141 FAGIYEEAFN GSWSTKTNWL FHAVKHY

Fig. 16

CONVERGENT TGF- β AND INSULIN SIGNALING
ACTIVATE GLUCOSE-BASED METABOLISM GENES

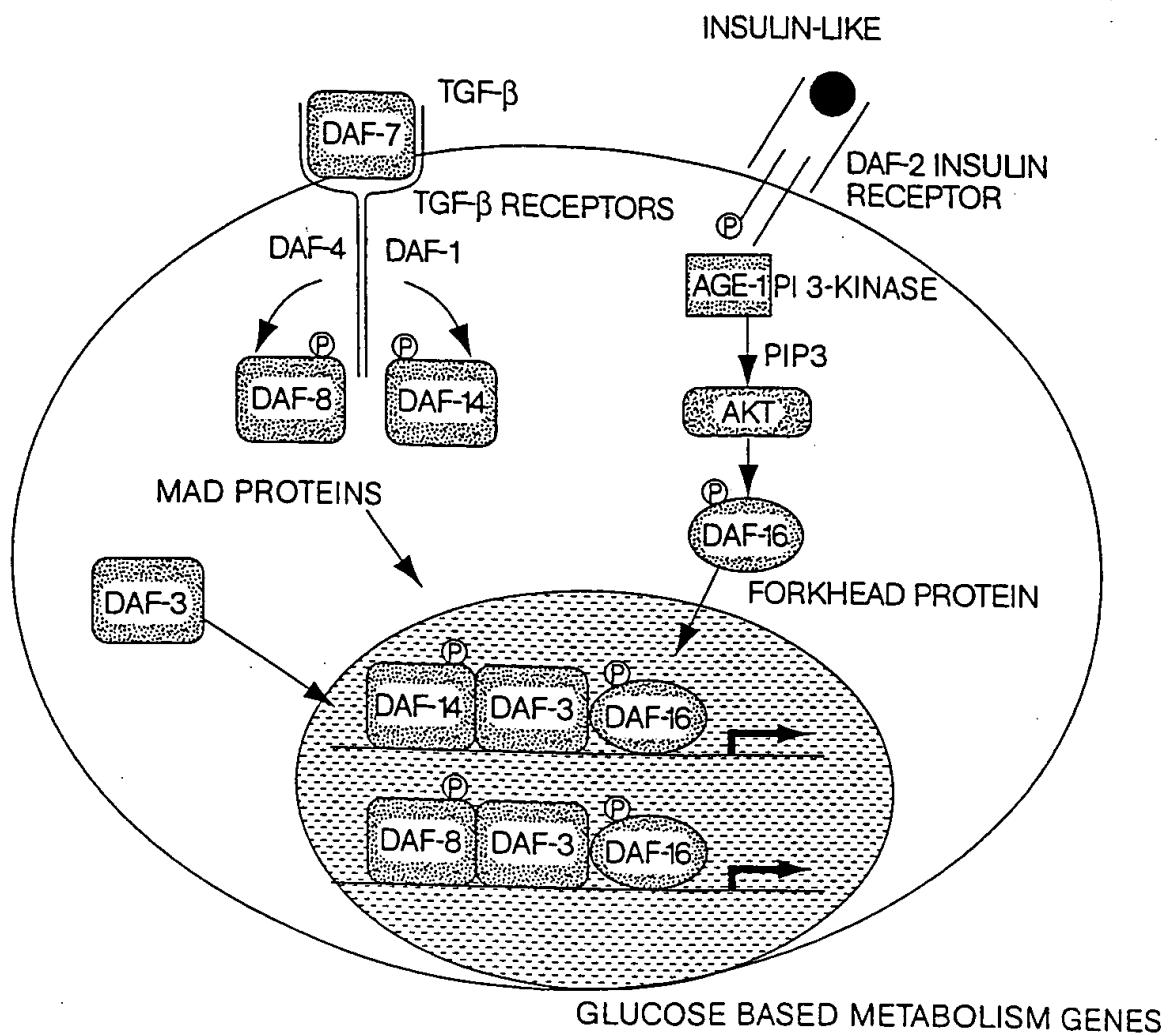


Fig. 17

IN PHEROMONE, NO TGF β OR INSULIN-LIKE SIGNALS
CAUSES REPRESSION OF ANABOLIC GENES

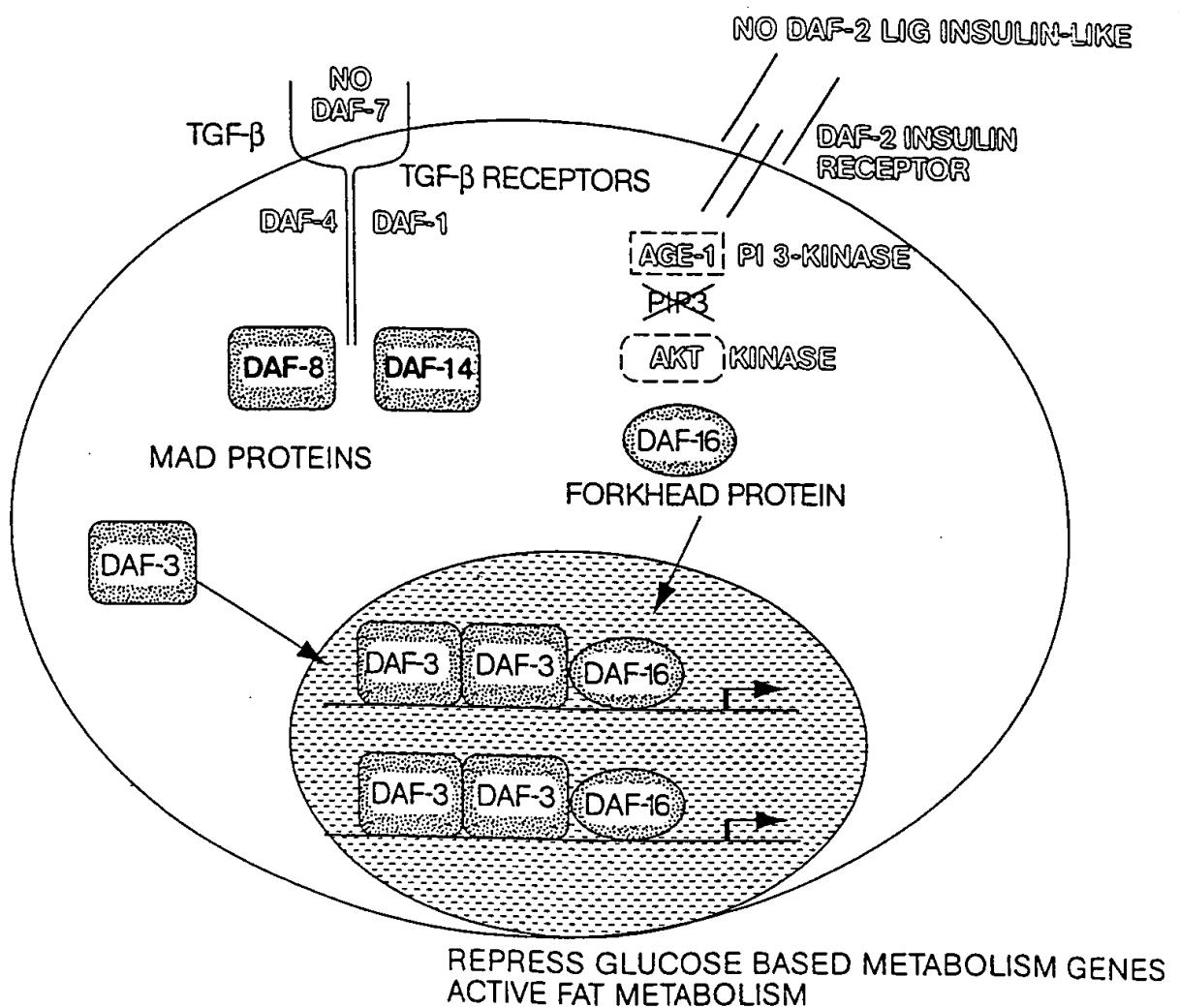
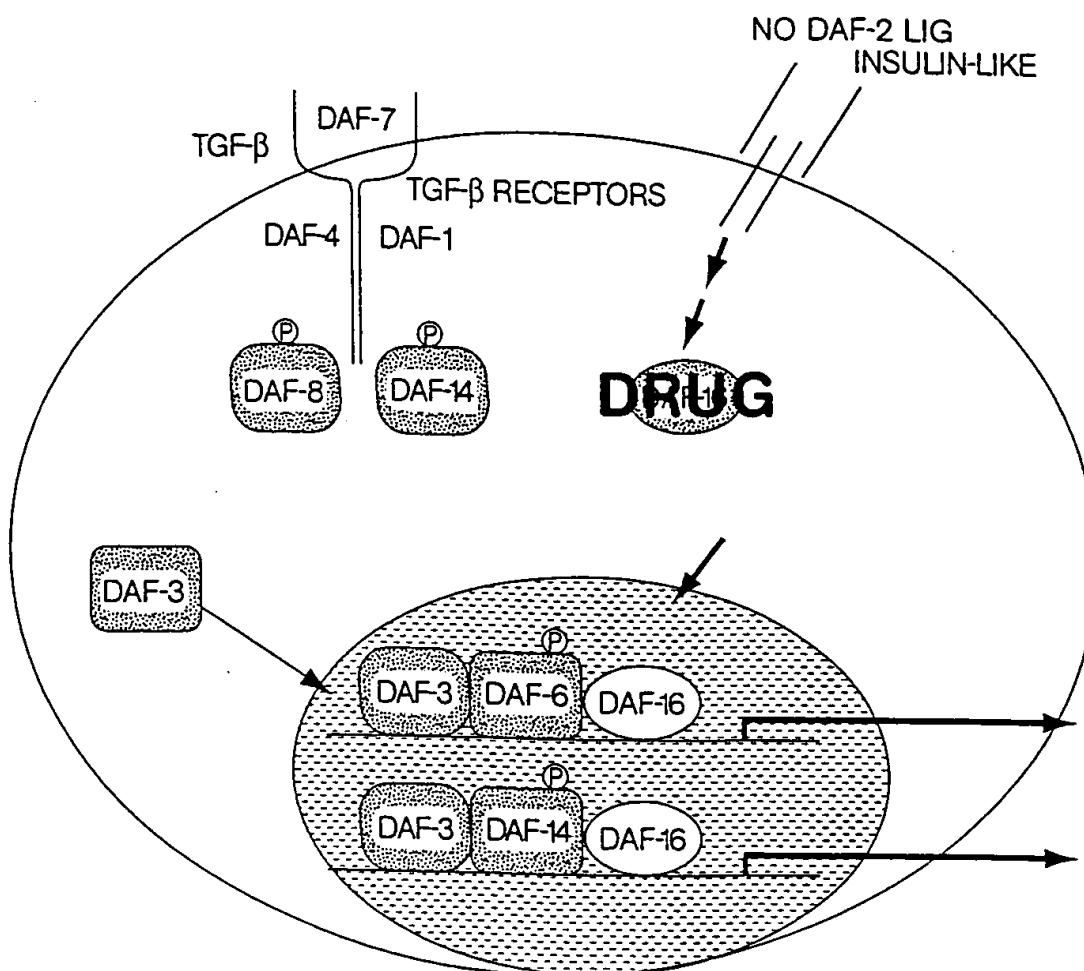


Fig. 18

DRUGS THAT INHIBIT DAF-16 OR DAF-3
(OR PROTEINS IN THE PATHWAY)
CAN BE DISCOVERED USING REPORTER GENES
BEARING THEIR COGNATE BINDING SITES



DRUG CAUSES A DECREASE IN DAF-16 ACTIVITY, ACTIVATING
THE REPORTER GENE LIKE A DAF-16 MUTANT.
THIS BYPASSES THE NEED FOR INSULIN

Fig. 19

DRUGS THAT INHIBIT DAF-3 WILL CURE
THE DIABETES CAUSED BY A LACK OF DAF-7

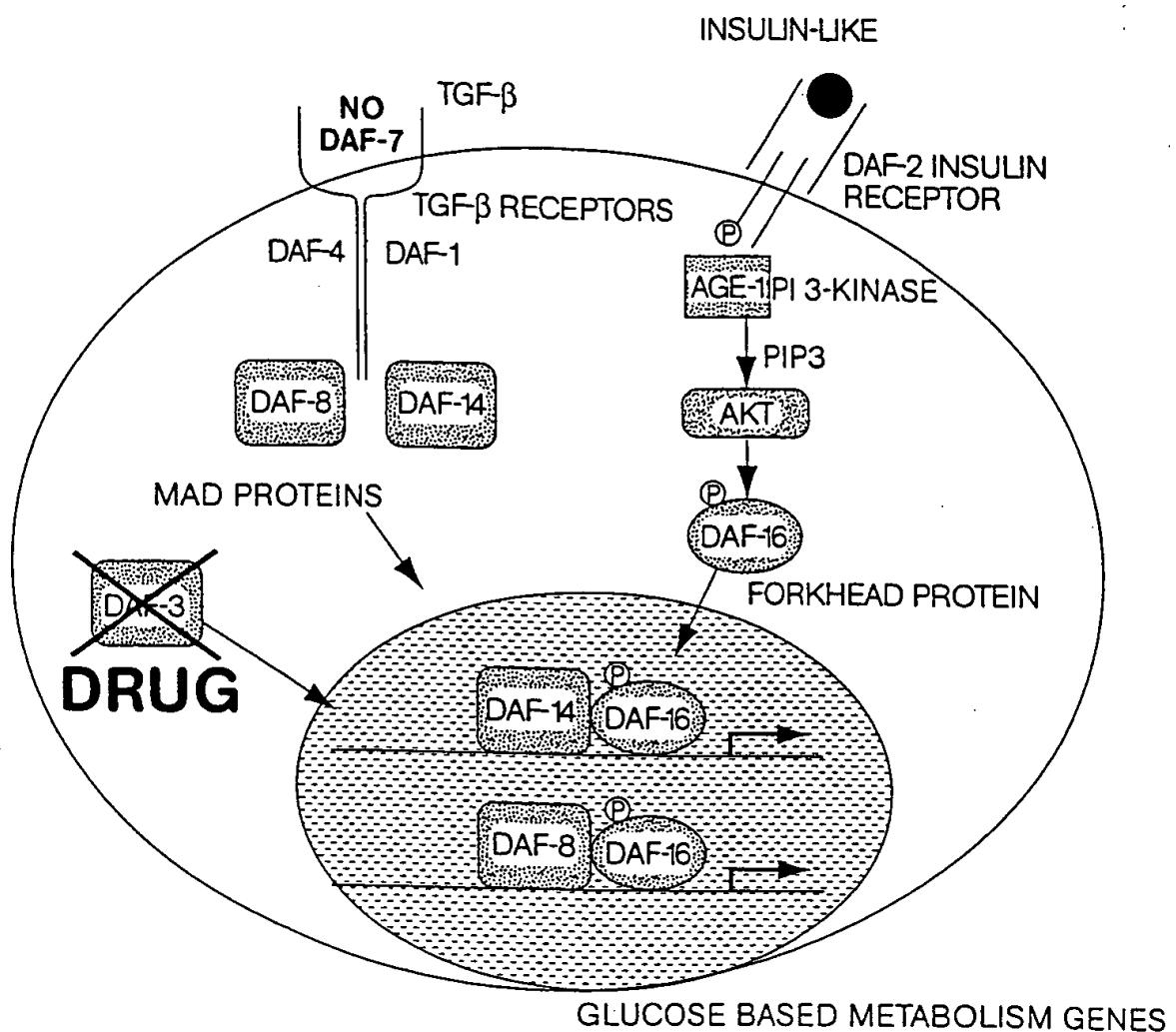


Fig. 20

ETG 21A-1

DAF-16a1	511	
DAF-16b	531	
FKHR	590	MGLLHQEKLPSDLQ. GMFIEREDCDMESTIRNDLWDCGETEDNETDVILENC.
FKHRL1	599	LPVMGHERFPSDLDLDMENGSELCDMESTIRSELMDADGLEDENEDSLISTONVGLNVGGNETGAKQASSQSWSWPG
AFX	502	

FIG. 21A-2

Fork head Domain Alignment (*C. elegans*, human, others)

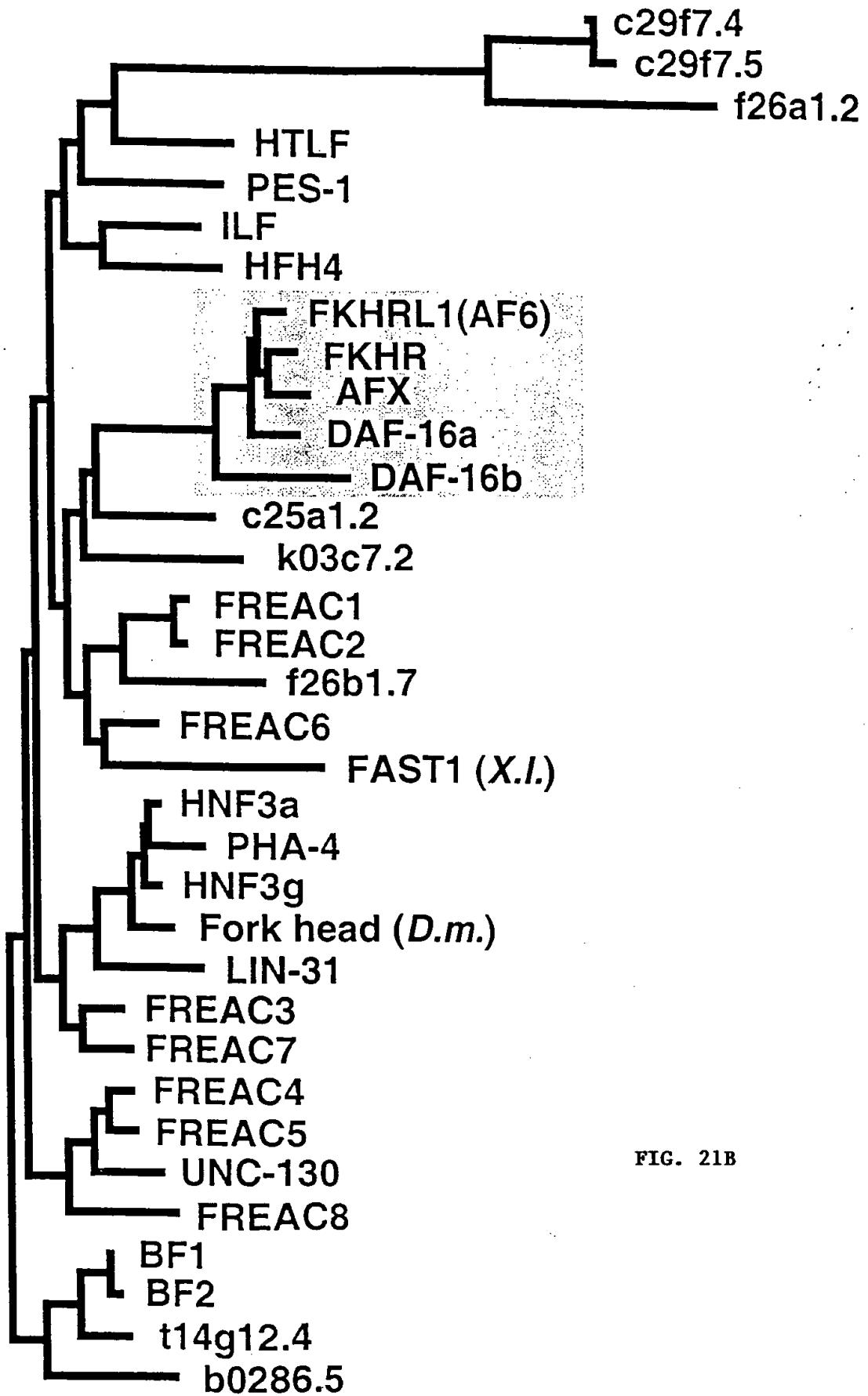


FIG. 21B

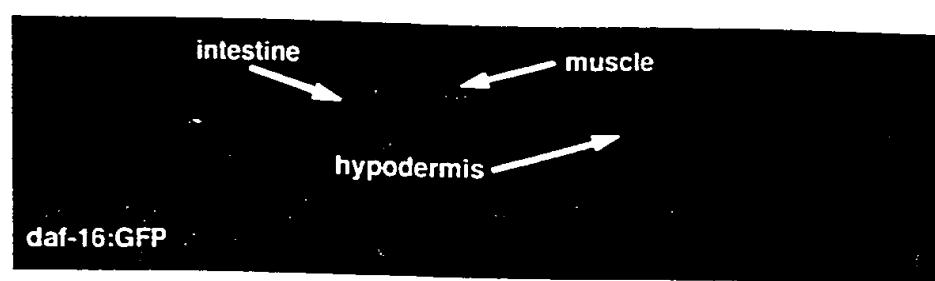


Fig. 22

INJECTION OF DAF-7 BYPASSES OBESITY-INDUCED DEFECTS IN INSULIN-REGULATION OF METABOLISM

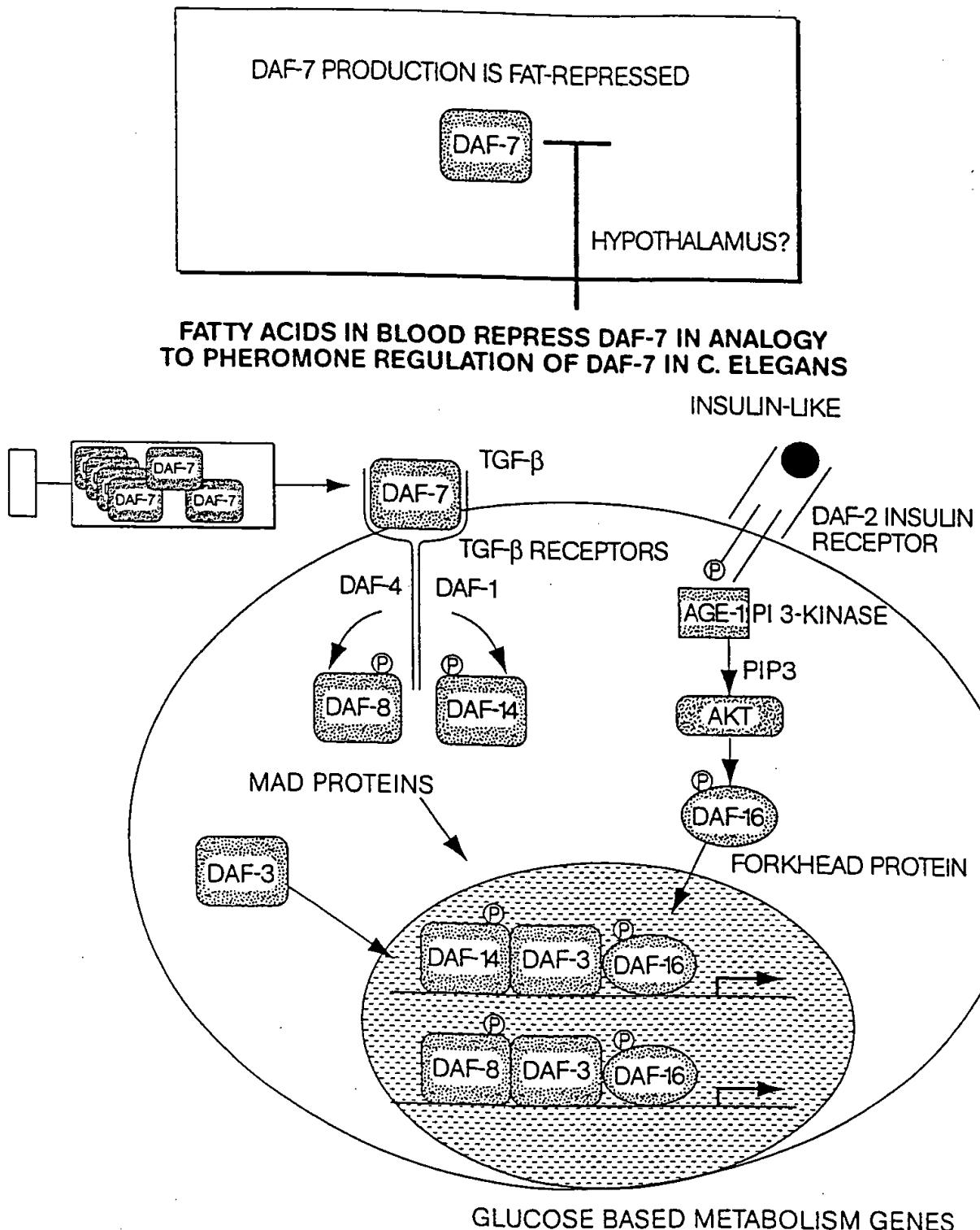


Fig. 23

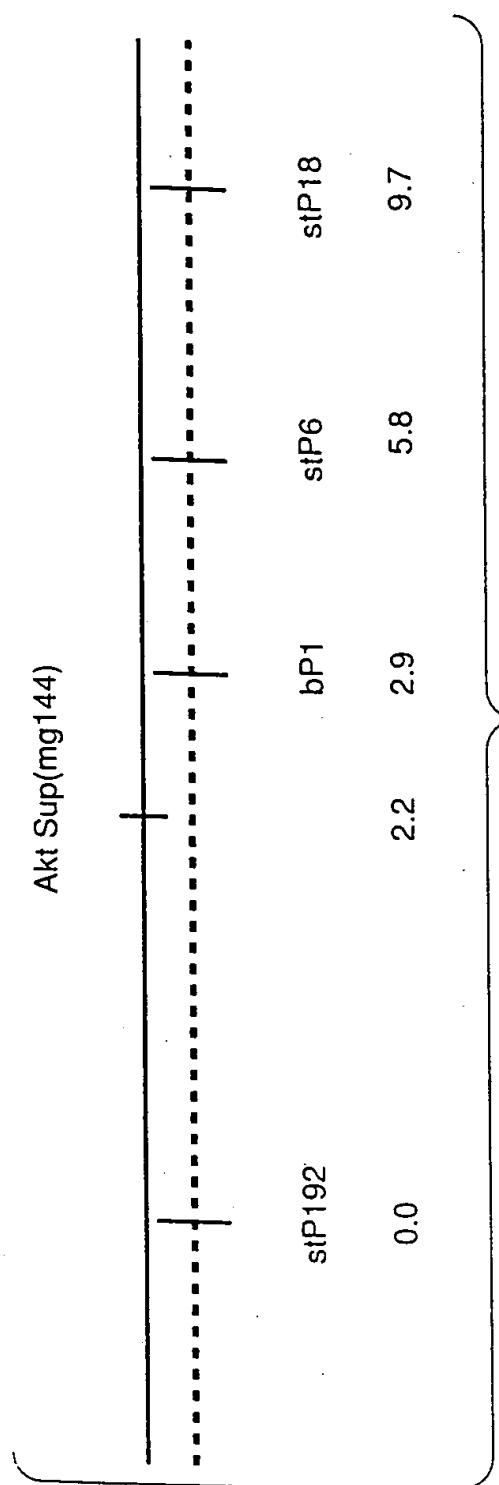


Fig. 24

Comparison of the human AKT protein sequence to the cosmid sequence C12D8, located in the genetic interval where sup(mg144) maps. Numbering in the AKT protein sequence by amino acid residues, and in the cosmid sequence by nucleotide position.

Score = 450 (207.4 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 79/121 (65%), Positives = 97/121 (80%), Frame = +1

335
 Query: 319 EVLEDNDYGRAVDWWGLGVVYEMMCGR LPFYNQDHEKLPELILMEEIRFPRTLGPEAKS 378
 +VL+D+DYGR VDWWG+GVVMYEMMCGR LPFY+DH KLFELI+ ++RFP L EA++
 Sbjct: 33685 QVLDDHDYGR CVDWWGVGVVYEMMCGR LPFYSKDHNKLPELIMAGDLRFP SKLSQEART 33864

Query: 379 LLSG LKKDPTQRLGGGSEDAKEIMQH RFF FANIVWQDVYERKLSPPFKPQVTSETDTRYFD 439
 LL+GLL KDPTQRLGGG EDA EI + FF + W+ Y K++ PP+KP V SETDT YFD
 Sbjct: 33865 LLTGLLVKDPTQRLGGGPEDALEICRADFFRTVDWEATYRKEIEPPYKPNVQSETDT SYFD 34047

Score = 256 (118.0 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 48/66 (72%), Positives = 59/66 (89%), Frame = +1

336
 Query: 146 TMNEFEYLKLLGKGTFGKVILVKEKATGRYYAMKILKKEVIVAKDEVAHTLTENRVLQNS 205
 TM +F+++LK+LGKGTFGKVIL KEK T + YA+KILKK+VI+A++EV AHTLTENRVLQ
 Sbjct: 32314 TMEDFDLKV LGKGTFGKVILCKE KRTQKLYAIKILKKDVI IAREEV AHTLTENRVLQRC 32493

Query: 206 RHPFLT 211
 +HPFLT
 Sbjct: 32494 KHPFLT 32511

Score = 190 (87.6 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 36/45 (80%), Positives = 37/45 (82%), Frame = +2

339
 Query: 276 KLENLMLDKDGHIKITDFGLCKEGIKDGATMKTFCGTPEYLAPEV 320
 KLENL+LDKG DGHIKI DFGLCKE I G TFCGTPEYLAPEV
 Sbjct: 33509 KLENL LLDKG DGHIKI AD FGLCKEEISFGDKTSTFCGTPEYLAPEV 33643

Score = 188 (86.7 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 37/57 (64%), Positives = 42/57 (73%), Frame = +3

160
 Query: 209 FLTALKYSFQTHDR LCFVMEYANGGELFFHLSRERVFS EDRARFYGA EIVSAL DY LH 265
 + LKYSFQ LCFV M++ANGGELF H+ + FSE RARFYGA EIV AL Y LH
 Sbjct: 32667 YFQELKYSFQEQHYLCFVMQFANGGELFTHVRKCGTFSE P RARFYGA EIVL AL GY LH 32837

Score = 166 (76.5 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 29/59 (49%), Positives = 42/59 (71%), Frame = +1

161
 Query: 53 NNF SVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFH VETPEER EEWATAI QTVA DGLK 111
 + F++ Q M E+PRPN F++RCLQWTTVIERTF+ E+ E R+ W AI+ + + K
 Sbjct: 31846 STFAI FYFQTM LFEKPRPNM FMV RCLQWTTVIERTFYAE SAEV RQR WIHAI E SIS KKYK 32022

162
 Score = 134 (61.8 bits), Expect = 5.2e-167, Sum P(8) = 5.2e-167
 Identities = 24/33 (72%), Positives = 30/33 (90%), Frame = +3

162
 Query: 210 LTALKYSFQTHDR LCFVMEYANGGELFFHLSRE 242
 L LKYSFQT+DRLCFVME+A GG+L++HL+RE
 Sbjct: 33156 LQELKYSFQTNDRLCFVMEFAIGGDLYYHLNRE 33254



Fig. 26A

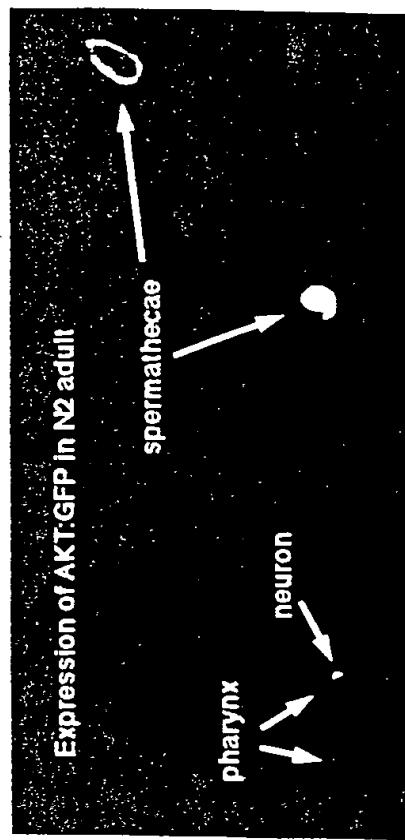


Fig. 26B

T G A C G T C G A C T G T G G T G

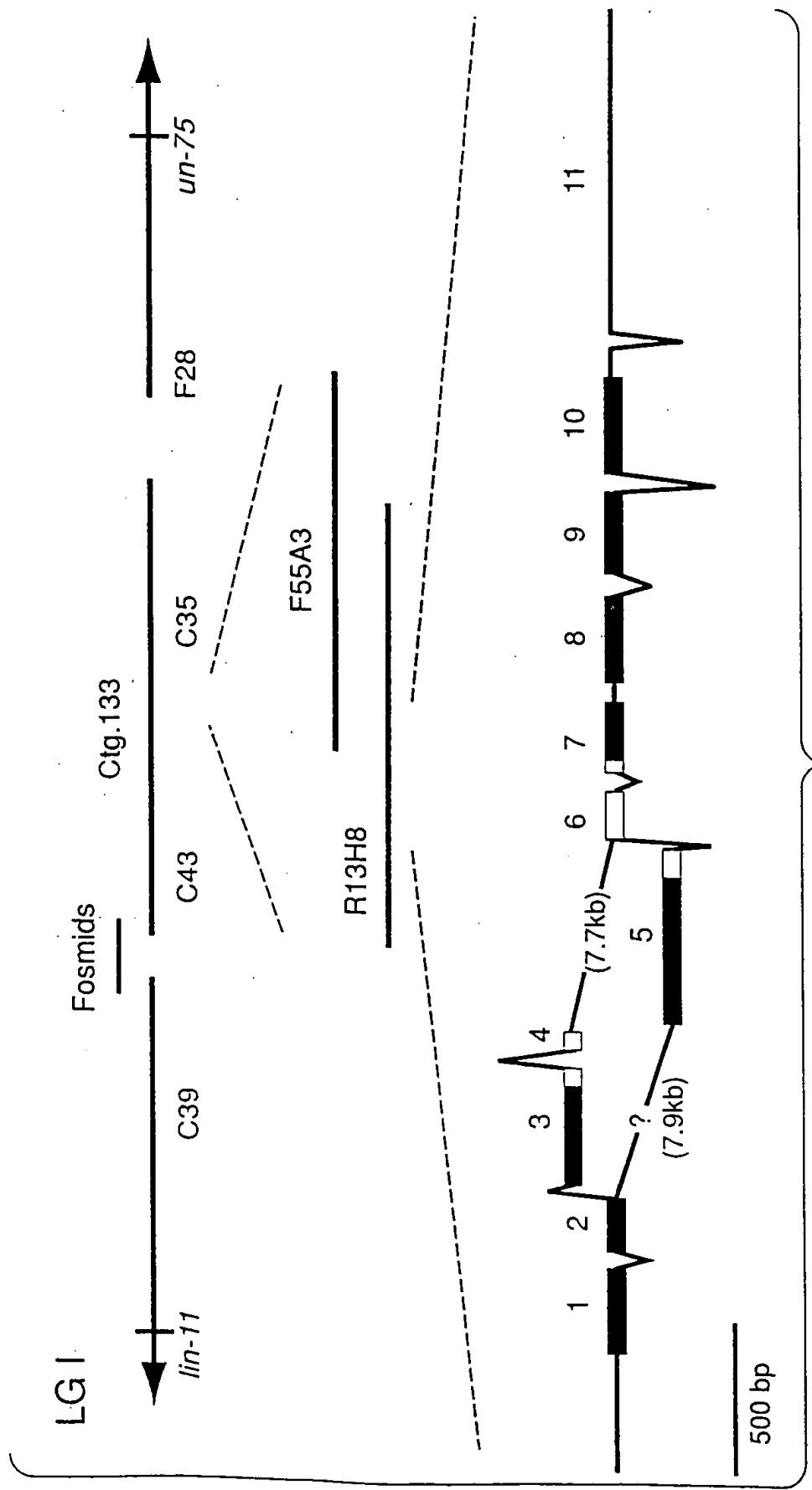


Fig. 27

	1	15 16	30 31	45 46	60
1 ZK84.6	-MNSVFTIIFVLCAL	QVAASFRQSF	G---P	SMSEESASMQLLREL	QH--NMME SAHRPMP
2 ZK75.1	-MFSFFT-YFLLSAL	LLSASC RQ	-----P	SMDT-SKADRILREI	E---MTELENQLS
3 ZK1251.2	---MPPILVFFLV	LIPASQQY	-----P	FSLE-SLNDQIINEE	VI--EYMLENSIRSS
4 C06E2	--MIVTLIVFLVIGL	QMAHLSQVSGNNENG	FLNP-FDLSQWSEEI	LHRQYHHHHHHHG	57
5 ZK75.2	---MNAIIFCLLFT	TVTATYEVF	-----G	KGIEHRNEHLLIINQL	D---IIPVESTPTPN
6 ZK75.3	MKLSVVLAFLIFQL	GAASLMRN	-----W	MDFEKELEHDYDDS	E---IGFHNIHSLMA
7 C17C3	-----	-----	-----	MKLHI	F---IIFLLFQSCSN
8 F13B12	-----	-----	-----	MYWFRQVYRPS	FF--FGFLAILLSS
9 INSULIN	-----	-----	-----	MA	LWMRLLPLLALLALW
CONSENSUS	-----	-----	-----	-----	17

	61	75 76	90 91	105 106	120
1 ZK84.6	RARRVPAPGETRACG	RKLISLVMACGD-L	CN-----	-----	85
2 ZK75.1	RARRVPA-GEVRACG	RRLLLFWWSTCGE-P	CT-----	-----	77
3 ZK1251.2	RTRRVDPDEKKIYRCG	RRIHSYVFAVCGK-A	CE-----	-----	78
4 C06E2	RARRTLETEKIYRCG	RKLYTDVLSACNG-P	CE-----	-----	88
5 ZK75.2	RASRVQK---RLCG	RRLILFMLATCG--E	CD-----	-----	74
6 ZK75.3	RSRRGDK---VKICG	TKVLKMMVMVMCGG-E	CS-----	-----	79
7 C17C3	KMCQYSK-KKYKICG	VRALKHMKVYCTR-G	MT-----	-----	48
8 F13B12	PTPSDAS---IRLCG	SRLTTTLLAVCRNQL	CTGLTAFKRSADQSY	APTTRDLFHIHHHQ-	80
9 INSULIN	GDPAAAFVNQHLCG	SHLVEALYLVCGERG	FFYTPKTRREAEDLQ	VGQVELGGPGAGSL	77
CONSENSUS	-----CG	-----C-----	-----C-----	-----C-----	

B CHAIN

C PEPTIDE

	121	135 136	150 151	165 166	180
1 ZK84.6	-----PQE GKDIA	TECCGNQCSDDYI	RS ACCP-----	112	
2 ZK75.1	-----PQEDMDIA	TVCCTTQCTPSYIKQ	ACCPEK-----	106	
3 ZK1251.2	-----SNTEVNIA	SKCCREECTDDFIRK	QCCP-----	105	
4 C06E2	-----PGTEQDLS	KLCCGNQCTFVEIRK	ACCADKL--	118	
5 ZK75.2	-----TDSSEDLS	HICCIKQCDVQDIIR	VCCPNSFRK	106	
6 ZK75.3	-----S-TNENIA	TECCEKMCTMEDI	TT KCCPSR-----	107	
7 C17C3	-----R-DYGKLL	VTCCSKGCNAIDIQR	ICL-----	73	
8 F13B12	-----KRG GIA	TECCEKRC SFAYLKT	FCCNQDDN-----	109	
9 INSULIN	QPLALEGS LQKRGIV	EQCCTSICSLYQLEN	YCN-----	110	
CONSENSUS	-----CC	-----C-----	-----C-----	-----C-----	

A CHAIN

Zk75-1	ACGRREFLLEFV	WSTCGGEPEPCTK	xxQEDMDIAT	YTKQAC	C46
Zk84-6	ACgrkHsyy	maVggd1cnx	xxqegkdiat	Yersac	C46
Zk1251-2	RCGCRKLEYTDV	FAVCGKACEX	xxSTEVNIAS	YFRKQ	C46
C06e2	RCGCTKVLKMY	LSACNGPCEX	xxGTEQDESK	FEIRKAC	C46
Zk75-3	1cggrrilfim	MVMGGECSX	xxSTNENIAT	DTTTC	C46
Zk75-2	1cgshlveaf	latcggedtx	xxDSSEDISH	ECCEKMQCTME	C46
Ins-Human	1ccSHlveaf	YLVCCERGFX	xxLQKRGTVE	QLEN	TC46
Ins1-Rabbit	1cgshlveaf	ylvcgerrgfk	xxtpksggiv	QCTSI	CSLY
Ins1-Xenopus	1cgshlveaf	ylvcgdrgrfx	xxkmtkrqiv	Qctsics1Y	46
Ins2-Xenopus	1cgshlveaf	ylvcgdrgrfx	xxkmmkrqiv	Qchntcs1F	46
Ins -Alligator	1cgshlvdai	ylvcgerrgfk	xxspkpggiv	Qchntcs1Y	46
Ins -Elephantfish	1cgshlvdai	yfvccgerrgfk	xxpkqgqgiv	Qchntcs1V	46
Igf1-Bovine	1cgAE1VDAI	QFVCCDRGFX	xxAPQTCIVD	ECCFRSCDLR	RREMY
Igf2-Horse	1cgelvdai	qfvccgdrgrfx	xxapqqtgiv	eccfrscdir	REMY
Igf2-Human	1cgelvdai	qfvccgdrgrfx	xxrrrsrgiv	eccfrscdla	1REMY
Irp-Amphioxus	1ccGSTLADV	QFVCCGDRGFX	xxRRRSGIVE	ECCFRSCDLA	1RETY
Lirp-Locust	1ccKELESNAE	SFVCCGNRGYX	xxRRRGIVE	ECCYNVC	DYS
Bxa4-Bommo	YCCGRHART	KLVCGRGNYNX	xxRRTRGVED	QEST	YC46
Bxb1-Bommo	YCCGRHADT	ADICWEAGVX	xxRGKRCIVD	ECCRKS	CSIS
Bxpa-Hornworm	YCCGRHart	ADICFGVEKK	xxRGKRCIVD	ECLRPC	SVD
Bxa1-Silkworm	ad1cpnveyx	ad1cpnveyx	xxgkkrqgva	ECCFRP	CTLD
Bxa2-Silkworm	sfvcdnqyqkx	sfvcdnqyqkx	xxgkkrqgiae	VLSY	C46
Bax3-Silkworm	LYVCDNQYQX	LYVCDNQYQX	xxgkkrqgiae	VLSY	C46
Mpi3-Sea snail	YCCGRRIATM	YCCGRRIATM	xxgkkrqgiae	CCNKPCTEN	ELKTE
Relaxin-Human	SY1CCRNQLCX	SY1CCRNQLCX	xxgkkrqgiae	CCNKPCTED	ELLAY
Rlf-Human	QWICSTANMV	QWICSTANMV	xxgkkrqgiae	CCFNQCTVQ	ELAY
	IAHCCGREVRAO	IAHCCGREVRAO	xxgkkrqgiae	CCCLIGCTKR	SEAKY
	1cgghfvrat	1cgghfvrat	xxaaatnpar	YCC1sgctqq	dl1t1
					C46

Fig. 29

TOP SECRET//SI

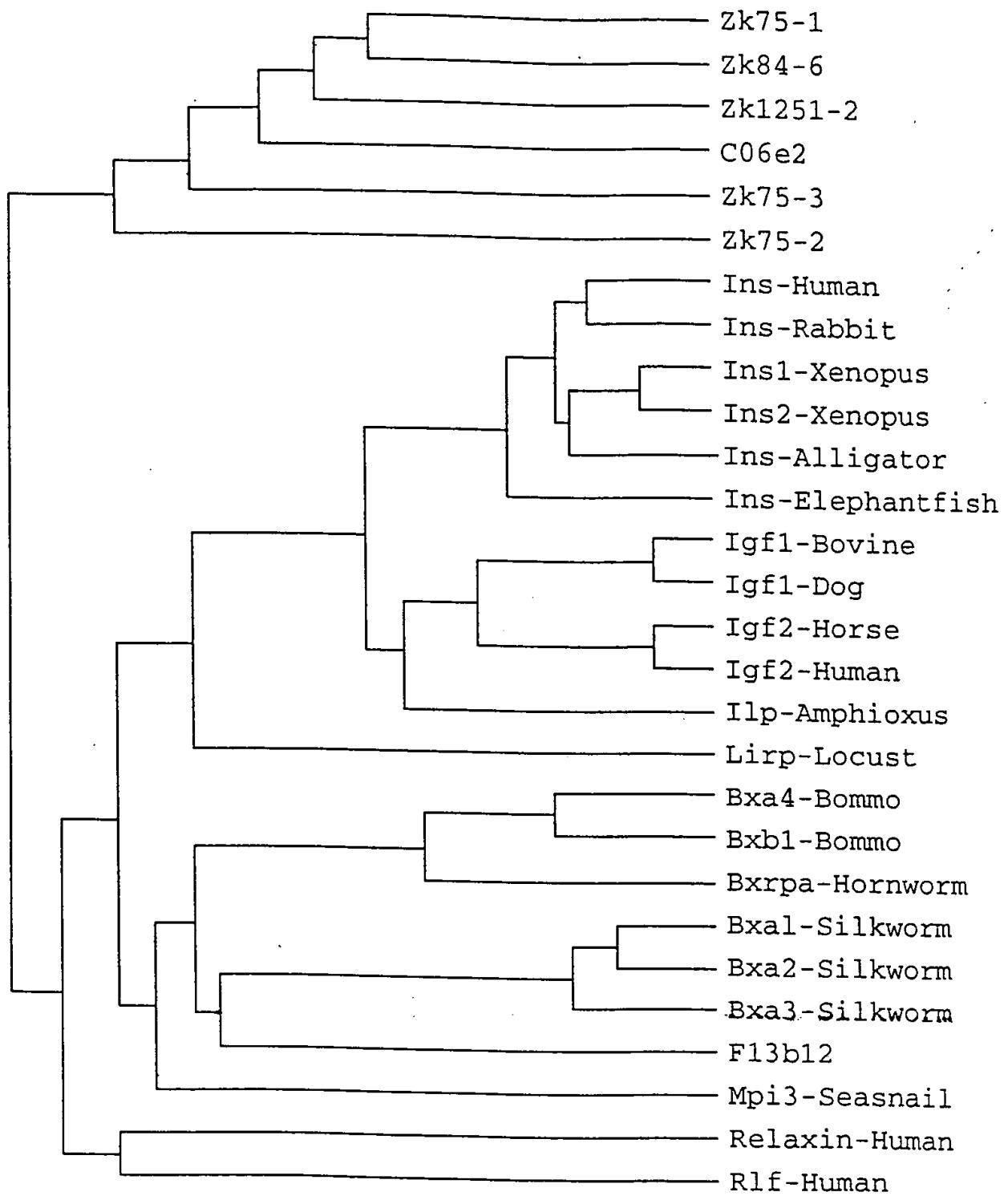


Fig. 30

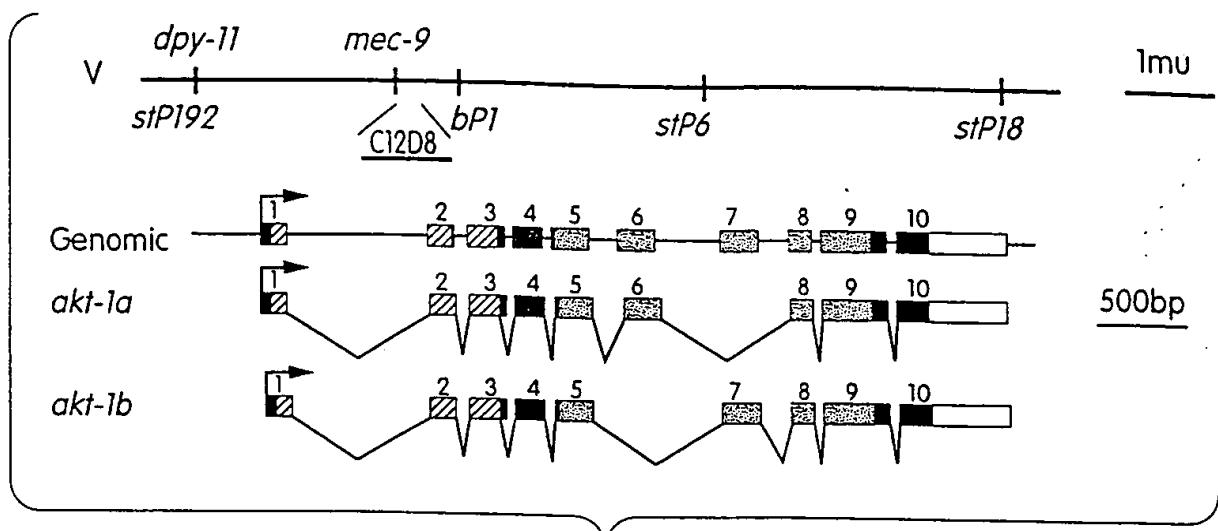


Fig. 31

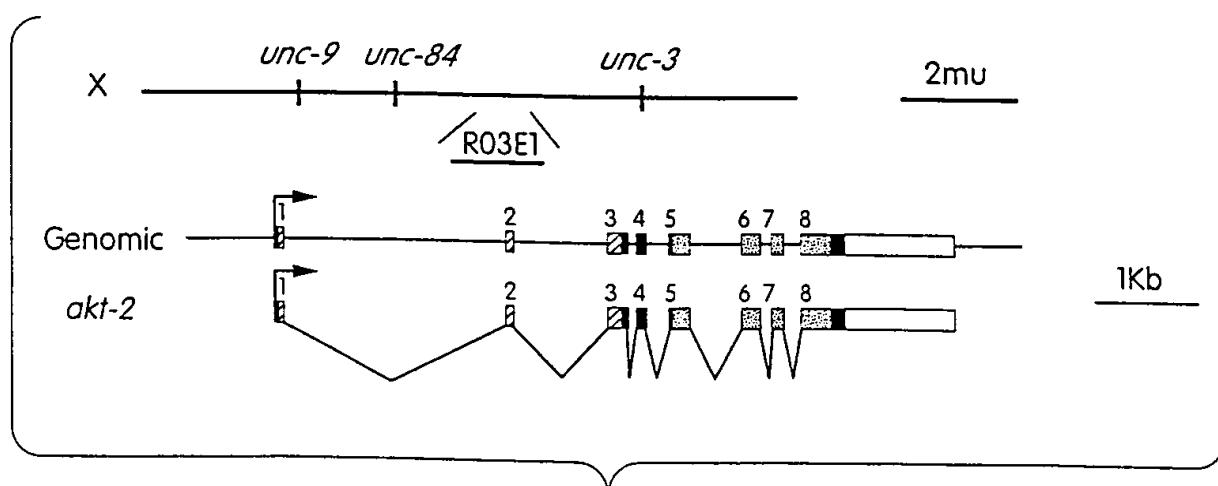


Fig. 32

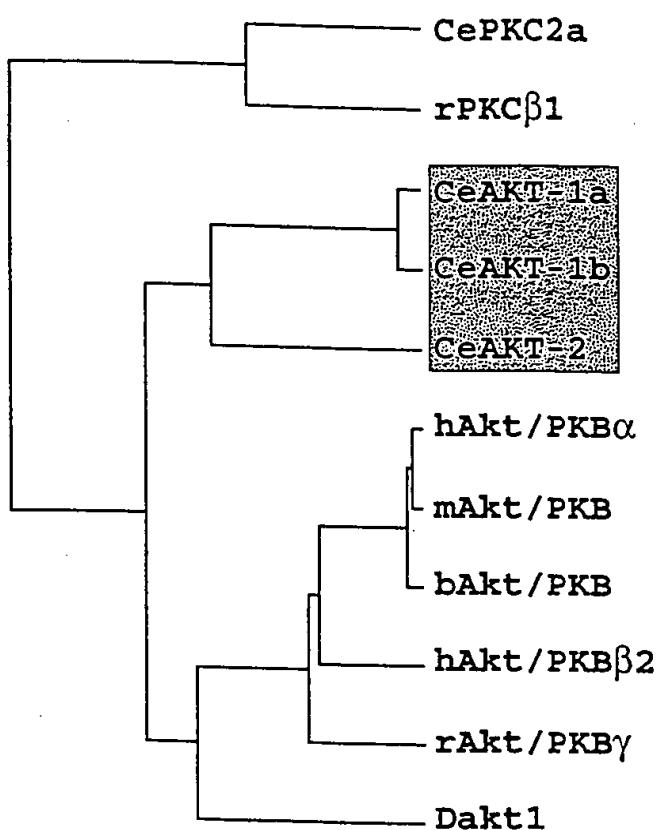


Fig. 33

AKT-1a	MSMTSLSTKSRR--QEDVVIEGWLHKKGEHIRNWRPRYFMIENDGALLGERAKPKECOPFPEPL
AKT-1b
AKT-2	M..ENAHLQK..I...S..
hAkt/PKBa	MSDVAL..K..R..Y..KT..LLK..TFT..YKER..QDVEDOREA..
AKT-1a	NDFMIKDAATMLFEKPRPNMFMRCLQWTTVIERTFYAESAEVRQRWIAHESI-S--KVKGTN
AKT-1b
AKT-2	N..R..VCLD..I..D..DF..E..QAV..SHNRL..ENA
hAkt/PKBa	N..SVAQCOL..KT..R..T..H..HV..TP..E..EE..TT..OTVADGL..KQE--
AKT-1a	ANPQEELMETNQQPKIDEDSEFAGAAHAIMGQPSSGHGDNCISIDFRASMISIADTSEAARKDKI mg144 T
AKT-1b
AKT-2	G..TSMQEED..GN..SGES..VNM-----DAT..TRS.....ESTVMN..DEPE..V..RKNTV
hAkt/PKBa	-----E..EMD..-----R..GSPS..SGAE-----EMEV..L..KPKHRV
AKT-1a	TMEDEFDELKVLGKGTEGKVILGKEKRTOKLYAIKIKKKDVIAREEVAVTLTENRVLGRCKHPE
AKT-1b
AKT-2	..D..Q..R..SSD..IR..EMVVD..S..V..A..V
hAkt/PKBa	..NE..EY..L..V..A..GRY..M..E..V..KD..NSR..
AKT-1a	LTELKYSEOEQHYLCEVMOFANGGELETHVRK--CGTSEPRARFYGAELVLAGGYLH..RC
AKT-1b	TNDR..E..I..D..YV..LNREVOMNKEG..S..AN
AKT-2	L..A..VHL..E..I..LQR..K..A..T..S..HR
hAkt/PKBa	A..THDR..EY..F..LSRE..RV..D..S..D..SEK
AKT-1a	DIVYRDMKLENLLDKDGH..K..IADFGCLKEEISFGDKTSTFCGTPEYLAPEVLDHDYGRCVDW
AKT-1b	S..L..
AKT-2	N..R..T..KY..I..E..L..D..S..
hAkt/PKBa	NY..L..M..T..G..KD..ATMK..E..N..A..
AKT-1a	WGVGVVMVEMMCGRLPFYSKDHNLFEELIMAGDLRPSKL'SOEARTLITGLLVKDPTQRLGGGP
AKT-1b
AKT-2	SA..ENG..TTC..K..NR..P..V..S..ERV..AK..A..
hAkt/PKBa	L..NQ..E..LMEET..RT..GP..KS..S..K..K..S..
AKT-1a	EDALEICRADFERTVDWEATYRKEIEPPYKPNVQSETDTSYFDN-EFTSQPVQLTPPSRSGALA
AKT-1b
AKT-2	D..R..VS..E..KD.....L..V..F..M..F..RVRYV..ILLKV----.E..I
hAkt/PKBa	K..MQHR..AGIV..QHV..E..KLS..F..Q..T..R..E..A..MITI..DQDDSM
AKT-1a	TVDEQEEMQSNTQSFHNVMGSIINRIHEASEDNEYDMGZ
AKT-1b
AKT-2
hAkt/PKBa	C...-S..RRPH..P...YSASSTA

Fig. 35A

attttggtagttgacatgaaactttaaaaactgaatacgtatTTcaacttacagggtgcgcgacccgagtacccgtatcaccagtcaagaact
 tatggctcacaagttttgaaaacgttgaactgggtgaacattgcaaataatcaagccaccagtccgtcacgcctacattccagccacattggcg
 agccggagtactactctaacattggcctgtcgagccggacttgcgtatcGTGCCCTGTTCCGTTGATGAATTGGAAATGATGCTAGCGCA
 TCACAGCCATCAACGTGAGTTGAAGCCTTTCTTGCAATTAAAGTTTACCTGCACTGACCAAAATTATTGAAACTATTATTATTGAA
 TTCTGATTAACAATGACCAAAAGATTGAACTGACAAAGTGCAATTGACCCACCAAAAAACGTTGCACTGACCACCTCTCATTGCACT
 GACCACCTCTCATTGCACTGACCAACTTCAATTGCACTGACCACCTCTCATTGCACTGACCCACCTTTCAATTGCAATTGCAATGAA
 TTCTTTGCACTACTGATCAAAAATTGATCAAATCAATTAAATTCTTGTACAGTACTATGCCATTCAAGGAGATGCTGATGAAATTC
 TCAATAGTTGATAAAAATTACTAACCCCTAGAAAGTTGACCCGTCTAACGTGGAACATCGGGAGACCCATTGTTGGAATTGCACTGCA
 GAGTGATTGACCTAATTGGTTATTTTAAATCATTAATTAGACGCCAATTGGAAAGGGAAACCGGCCACGTGCGCAGA
 AGCTCGAAGACCAACGTGTCAAAAACCCATTCCACATCTCACCAACAACTCGTCATTGAAACAAGGATATTGGAAAAGAAGCGAGGATTG
 TTTGCCAGACGCCGAATGTTCTGTTGACCGAAGGACCGCATCTCTGTACATTGATGTGCCGAATTGTGCTCAAAGGAGGGTACCATGGAC
 GCCGTGCTGCGAGGTGGAGCTAAAAAACTCGGAACATTCTTATACACGGTAGGTGAGAATTATCATAGCTGTCTATCTCATTATAGTACTC
 AATGAATCTGAAAATTCAAATTTCAGCCCAACCGCGTCTACTACTTGTGATCTCGAAAAGAAAGCAGATGAGTGGTGTAGGCTATCAATG
 ATGTTGCAAGCGGTACTCGGTGACTATCGAAAAGACTTTAACTCTGGATGCGTACCGGAACATTGGCAGCATTATGAAAGAAAAGTCC
 AGAAAGGTATGAATTACTGGAAGGCCCTCACTGAGTTCCAGAACGTTTGTGAAATTGGCAATTTCATTAGACTTAA
 GAGCCTATTGCTATTGTTGGAAGGTTAAACATTTCAAAAAAATTGAGAAATGCTGAAAAAATTGGAGTGTGACAGTTCTGAAATT
 TGAAAATTCTGTTCTCAAAATTGGATTTCAGAGCTGTTGAGATTTCATAATCCTTCAAAAGAATATAGAATATTGTTGTTCAACTTTTC
 TTGTCAAAATTATTGGACAATTGAGATTCTGGAAAATTTCAAAAAAAGATAATCTCTAACACAAACTAAATTCAAAATGTTCTAAAGGT
 TCTTATTTCATGCAACTCTAAAATTCTCCGTATATTGGAAAGTCTTGTGTTAGACGGTTAAATTGGATGTTGAAATT
 TTTAGGGGTGGTCTATAATTGGACCACCCGTATAATTGACCCACCATGTACACTTATAGACCCAGTAACAAGCATTGGACCA
 CACGCAATTCTTATTATTGGACCAACTTAGAACACCTCAAAACTCTTGTGTTCAAAAATGATCAACTTGTGTTGAAAAAATT
 TTTGAGGAATGATGCGTGAAAGAAGCGCTGCGCCGAAACAAGAAAAGGAGGAGAAAAGGCCTAAAAGCCGAGCAAGTGAAGAAGC
 TTCAATGCAAAATTGGACAAGAAGTGCCTGAGGCTCACCTCCCTACTCCCCACAAAATGCAACTCAAACAAATCACACTTTGTATCATT
 TTGCGTCC

Fig. 35B

MEDLTPTNTSLDTTTNNDDTSREAAPTTLNLTPTASESENSLSPVTAEDLIAKSIKEGCPKRTSNDMFLQSMGEG
AYSQVFCREVATDAMFAVKVLQKSYLNRHQMDAIIREKNILTYLSQECGGHPFVTQLYTHFHDQARIYFVIGLV
ENGDLGESLCHFGSFDMILTSKFFASEILTGLQFLHDNKIVHNDMKPDNVLIQKDHILITDFGSAQAFGGLQLSQEGFT
DANQASSRSSDSGSPPPTRFYSDEEEENTARRTFVGTALYVSPEMPLADGDVGPQTDIWGLGCILFQCLAGQPPFRAV
NQYHLLKRIQELDFSFPEGFPEEASEIIAKILVRDPSTRITSQELMAHKFFENWDVNIANIKPPVLHAYIPATFGEPE
EYYSNIGPVEPGLDDRALFRLMNLGNDASASQPSTPSNVEHRGDPFVSEIAPRANSEAENRAARAQKLEEQRVK
NPFHIFTNNSLILKQGYLEKKRGLFARRMFLLTEGPHLLYIDVPNLVLKGEVPWTPCMQVELKNSGTFIHTPNR
VYLYFDLEKKADEWCKAINDVRKRYSTIEKTFNSAMRDGTFGSIYGKKSRKEMMREQKALRRKQEKEKKAL
KAEQVSKKLSMQMDKKSP

Fig. 36

MEDLTPTNTSLDTTTNNDDTSREAAPTTLNLTPTASESENSLSPVTAEDLIAKSIKEGCPKRTSNDMFLQSMGEG
AYSQVFCREVATDAMFAVKVLQKSYLNRHQMDAIIREKNILTYLSQECGGHPFVTQLYTHFHDQARIYFVIGLV
ENGDLGESLCHFGSFDMILTSKFFASEILTGLQFLHDNKIVHNDMKPDNVLIQKDHILITDFGSAQAFGGLQLSQEGFT
DANQASSRSSDSGSPPPTRFYSDEEVPEENTARRTFVGTALYVSPEMPLADGDVGPQTDIWGLGCILFQCLAGQPPFRAV
AVNQYHLLKRIQELDFSFPEGFPEEASEIIAKILVRDPSTRITSQELMAHKFFENWDVNIANIKPPVLHAYIPATF
GEPEYYSNIGPVEPGLDDRALFRLMNLGNDASASQPSTFRPSNVEHRGDPFVSEIAPRANSEAENRAARAQKLEE
QRVKNPFHIFTNNSLILKQGYLEKKRGLFARRMFLLTEGPHLLYIDVPNLVLKGEVPWTPCMQVELKNSGTFIHT
TPNRVYLYFDLEKKADEWCKAINDVRKRYSTIEKTFNSAMRDGTFGSIYGKKSRKEMMREQKALRRKQEKEE
KKALKAEQVSKKLSMQMDKKSP

Fig. 37

FIG. 38A

FIG. 38B

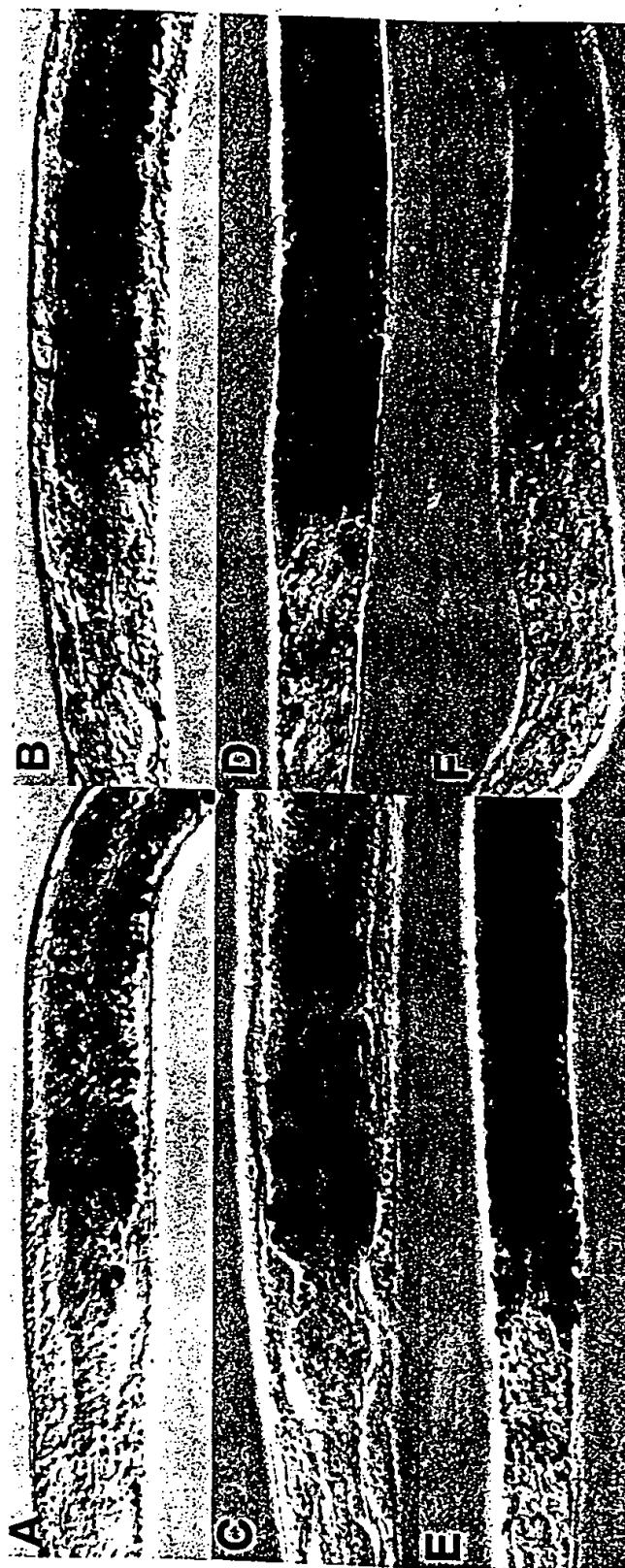


FIG. 38C

FIG. 38D

FIG. 38E

FIG. 38F

DAF-18

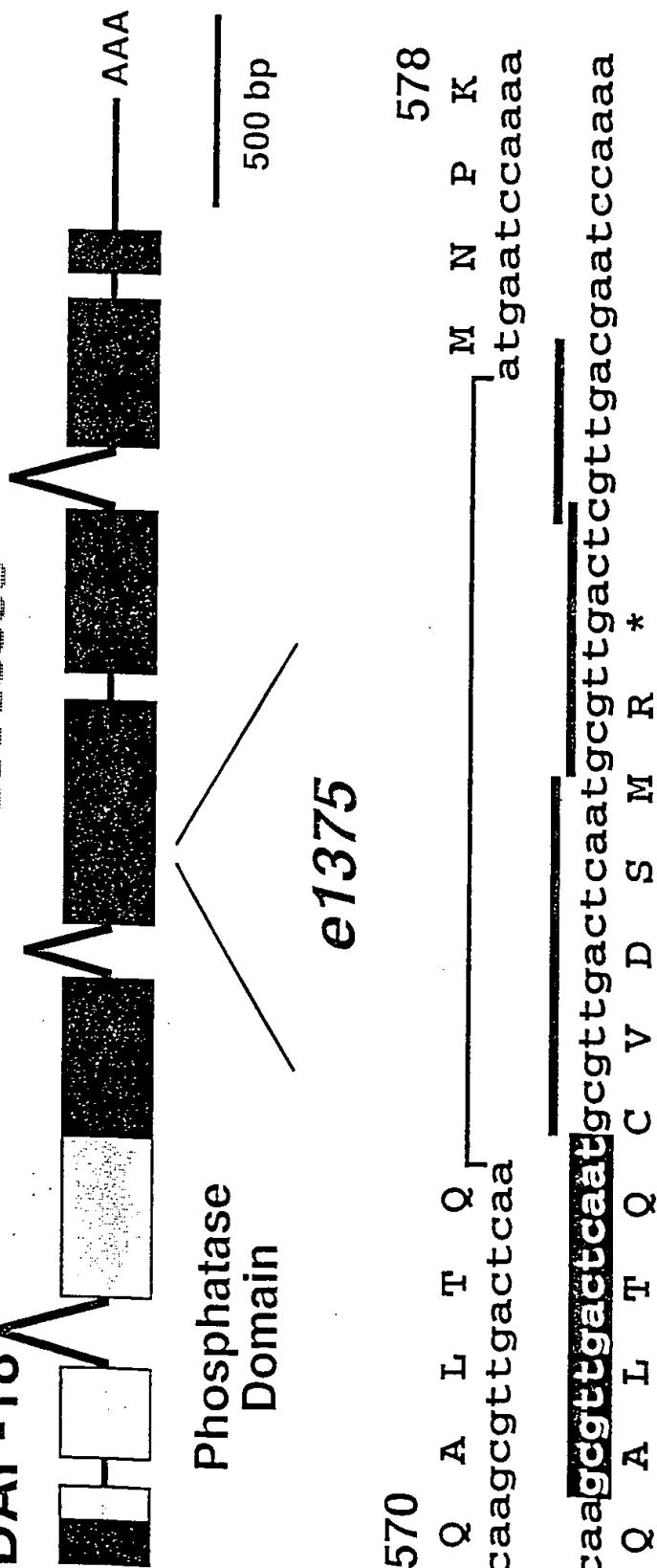


FIG. 39A

DAF-18	48	PFRTAVSSMR	CRETYQNTDL DCAYITDRI	AGYMPATGIE	ANFRNSKVQT
PTEN	4	LIKEIVSRNK	REYQEDGFDI	DLTXYTPNT	AMCFPAERIE
DAF-18	98	QOETTRPHGK	GNVKVENLRG	GYTDADNED	GNVICFDMID
PTEN	54	VRELDSEKHK	NHYKXNMCA	ERHYDTAKEN	CRVAQYPFED
<hr/>					
DAF-18	148	PFCREAKEWL	EADDKXHIAV	HCKACKGERG	WVICAKLTYI
PTEN	103	PFCECDDOWL	SEDDNHVAAT	HCKACKGERG	WVICAKLHR
DAF-18	198	DYSSILIFTKN	NKGVTIPSRQ	RYTYXHKEB	ERFLNLYFLR
PTEN	153	DFYGEVTRD	RKGVTIPSRQ	RYVYYSYEL	MQLIGVYVER
DAF-18	248	PFKTKWEGGSK	IKVEVNGST	ILFKPD.	EL LIISKSNHORE
PTEN	203	PFMFSEETCN	PQFVNCQLKV	RREDIKFMYFE	FPQFELIPVCGD

FIG. 39B

DAF-18 Protein

MVTPPPDPSTSTRSMARDLQENPNRQPGEPRVSEPYHNSIVERIRHIFRTAVSSNRCRTEYQNIIDLCAYITDRIIAIG
YPATGIEANFRNSKVQTQQFLTRRHGKGNVKVFNLRGGYYDADNFDGNVICFDMDTDHPPSLEMAPFCREAKEWLEAD
DKHVIAVHCKAGKGRGVMICALLIYINFYPSPRQILDYYSIIRTKNNKGVTIPSQRRYIYYYHKLRERELNYLPLRMQL
IGVYVERPPKTWGGGSKIKVEVGNGSTILFKPDPLIISKSNHQRERATWLNNCDTPNEFDTGEQKYHGFVSKRAYCFMVP
EDAPVFVEGDDVIRIDIREIGFLKKFSDGKIGHVWFNTMFACDGGLNGGHFEYVDKTQPYIGDDTSIGRKNGMRRNETPMRK
IDPETGNEFESPWQIVNPPGLEKHITEEQAMENYTNYGMIPPRYTISKILHEKHEKGIVKDDYNDRKLPMGDKSYTESGK
SGDIRGVGGPFEIPYKAEHVLTFFPVYEMDRALKSKDLNNGMKLHVVLRCVDTRDSKMMEKSEVFGNLAFHNESTRRLQA
LTQMNPKWRPEPCAFGSKGAEHYPPSVRYSSNDGKYNGACSENLVSDFFEHRNIAVLNRYCRYFYKQRSTSRSRYPRKF
RYCPLIKKHFYIPADTDVDENGQFFFHSPHEYIKEQEKİDAEKAAKGIENTGPSTSGSSAPGTIKKTEASQSDKVKPAT
EDELPPARLPDNVRRFPVVGVDFENPEEESCEHKTVESIAGFEPLEHLFHESYHPNTAGNMLRQDYHTDSEVKIAEQEAK
AFVDQLLNGQGVLQEFMQFKVPSDNSFADYVTGQAEVFKAQIALLEQSEDFQRVQANAEEVDLEHTLGEAFERFGHVVE
ESNGSSKNPKALKTREQMVKETGKDTQKTRNHVLLHLEANHRVQIERRETCPELHPEDKIPRIAHFSENSFSDSNFDQAI
YL

FIG. 40A

1 ttccaggatc atctactaac ccccaatgg tactcctcct ccagatgtgc caagcacatc
61 gaccaggatcg atggctcg accttcaaga gaatccaaac cgacaacctg gtgaaccacg
121 tgtgtctgaa ccgtatcaca attcaatcg cgagcggatt cgccatattt ttccggacgc
181 tgtatcttcc aatcggtgtc gcaccgagta cccaaatatac gacctagatt gtgcatastat
241 cacagaccga atcatagcta tcggttatcc agcaacagga atcgaagcga attccgtaa
301 ctcaaaaggt ccaaactcaac aatttctgac caggcggcac gggaaaggcga acgtgaaggt
361 gtttaacctg cgccgtggat actactacga tgcgataac ttcgatggaa atgttatttg
421 cttcgatatg actgatcatc atccgcccag tctcgaatta atggctccgt tttgcagaga
481 ggctaaggaa tggcttgaag cagacgataa acatgtataa gctgtacact gtaaagctgg
541 aaaaggccgt accggagtga tgatatgtc tcttctcatc tacatcaact tctatccgag
601 cccacgacaa attctcgact actactcaat aattcgtaca aaaaacaaca aagggtgtcac
661 aattccatca caacgacgct acatttacta ctaccataag cttcgtgaac gtgagctcaa
721 ctattnacca ttgagaatgc agttgattgg tgtctacgtg gaacggcctc caaagacatg
781 ggggtgggtt tcaaagataa aagtggaggt tggaaatggc tcgacaattt tatttaagcc
841 ggatcccttc ataatctcca aatcaaatca tcagcggagag cgtgcgcacgt ggctgaacaa
901 ctgtgatacg cctaacgaat tcgacaccgg agagaaaaa tatcatgtat ttgttccaa
961 gagagcatac tgttttatgg tgccagaaga tgctccagta tttgtcgaag gagatgttcg
1021 tatagacatt cgcgaaaatcg gatttctcaa aaagtttcg gacgggaaga ttggcatgt
1081 ttgggtcaat acaatgtcg catgtgatgg aggactcaac ggtggacatt tcgagttacgt
1141 agacaaaact cagccgtaca tcggagacga tacatcaatc ggacggaaaa atgaaatgc
1201 aagaaaatgaa acgcccgtatgc gaaaaatttg tccagaaact ggaaatgaat ttgagtctcc
1261 gtggcaaata gtgaatccctc ctggacttga aaaacatatt acggaggaac aagaatgg
1321 aaattatacc aattatggca tgattcttcc tcgatacacg atcagcaaga ttcttcacga
1381 aaagcatgaa aaaggatatcg tcaaggatga ctataatgtat cgtaagctgc caatgggaga
1441 caaatcatac acggaatcag gaaaaagtgg agatattcga ggagtcgtg gtccatttga
1501 gataccatat aaagctgagg aacatgttct cacatttcca gtttatgaaa tggatcgac
1561 attgaagagt aaagatctta acaacggaaat gaaacttcac gttgttctc gttgtgtaga
1621 tactcgat tcaaaaatgaa tggaaaagag cgaagtgttc ggcaatctgg cattccataa
1681 tgaatcgaca cggaggcttc aagcggttgc tcaaatgaat cccaaatggc gacctgaacc
1741 gtgtgcgttc ggatccaaag gtgctgaaat gcattaccct ccgtcggttc gatattcaag
1801 caatgatggaa aagtataatg gagcctgcag tgagaacattt gttagcgatt tttcgagca
1861 cagaaatatt gccgttctt atcgatattt ccgatatttc tacaagcaac gcagttacatc
1921 tcgaagccgt tatccaaagaa aattcagata ctgtcctctg atcaagaaaa atttctacat
1981 tccagctgat accgatgtatg ttgatgaaaa tggcaacccg ttcttccact caccagagca
2041 ttacattaaa gaacaggaaaa aatagacgc agagaaaagca gctaaaggaa ttggaaaatac
2101 tggaccctagt acttcaggat caagtgtcc cggaactatc aagaaaaacgg aagcttcac
2161 atccgacaag gtgaagccgg caactgaaga cgaacttctt cctgcgaggc taccggataa
2221 tgtgcgaaga ttccagtcg tcggcgttga ttgcggaaaat ccggaaagaag aatcgatgt
2281 acacaaaacc gtagagtcaa tagctggtt tgaaccactc gaacatctat tccatgaatc
2341 ataccatcca aatacggccg gtaacatgtc gcgtcaggat tattcacactg attccggaaatg
2401 gaaaatagct gaacaagagg caaaagccctt cggtgaccag ttgcttaatg gacaagggtgt
2461 attacaagag tttatgaagc aattcaaaatg accatcgac aattcccttg ctgattatgt
2521 aaccggacag gccgaagttt taaaaggcaca gattgcgtt a cttggagcagt cggaggattt
2581 tcaacgagtt caagcgaatg cagaggaatg cgatcttgc a cactcttgc tgaagcggtt
2641 tgagcgattt gggcacgtt gtagaagaatc gaatggttt tctaaaaatc caaaaggccct
2701 gaaaactcga gaacaaaatgg tggaaagaaaa tggcaaaagac actcagaaga cccgcaatca
2761 tgtgtttctt catttggaaag ctaatcatcg tgcgttgc gacgtgttgc aaacgtgccc

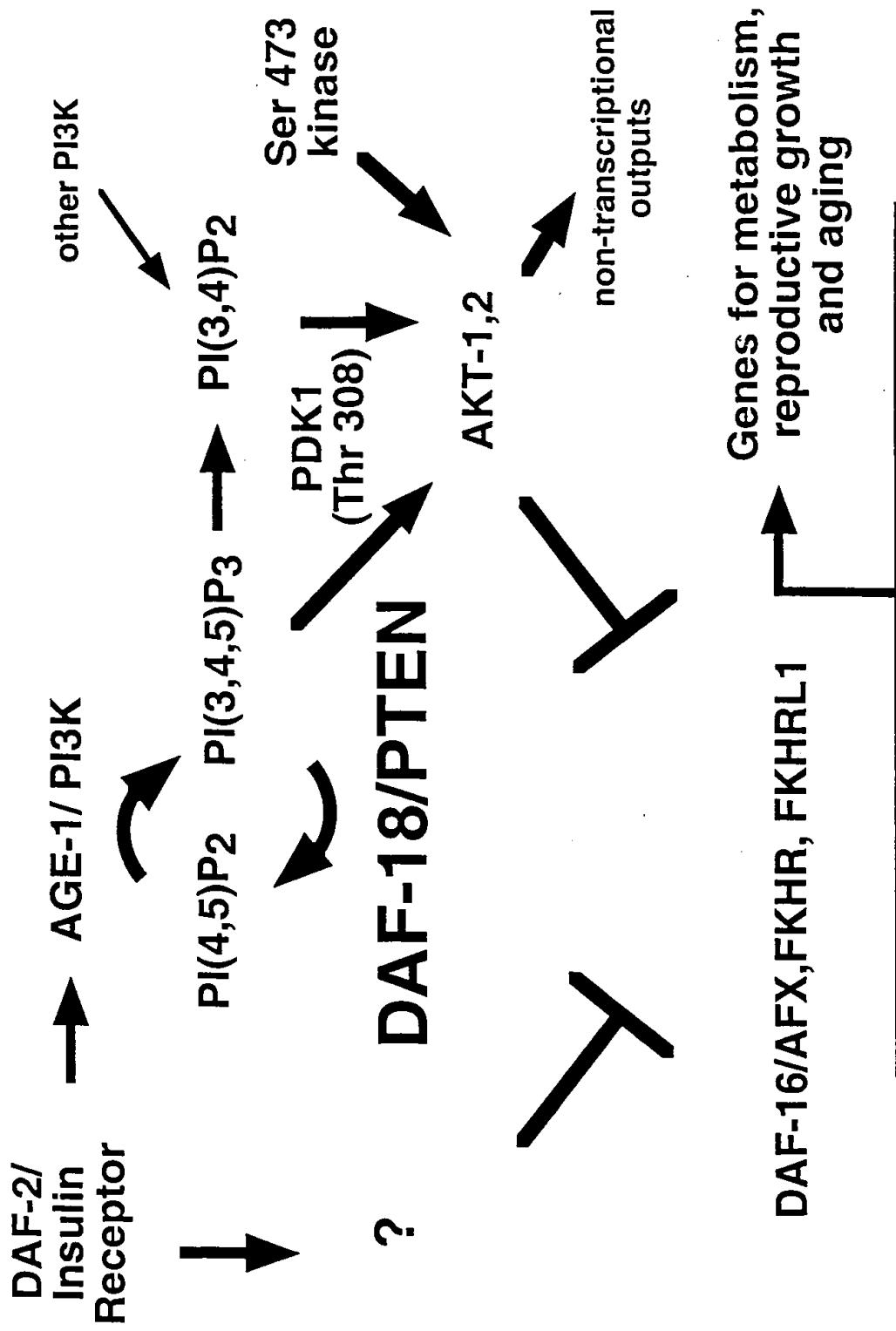
FIG. 40B

2821 ggagctacat ccagaggata aaatcccaag aattgctcat tttccgaaa acagcttctc
2881 ggattcgaat tttgatcaag ctatttattt gtaaacctaa aacaaaactt tttagaagatt
2941 ttcttcttac tgaccctcca atttcagat aatttcaatg ttttaagttt tctcttcaaa
3001 gtatcatcca ctttctgtat agtgtttgt ttttaacaa actattgttc gattattttg
3061 tatattcata ttatagtctc caacttcccg atttccacg tatatatgtt tattttgccc
3121 ggtaaaaat agcaattccc tatgaatgtt ccccttcca tctgtttct tactcagaaa
3181 ttgttaattca cattgcgggt catcaactaat cctatgggct ttaacacaat tctcccataa
3241 attaattgtt cttaccaatt ttttgtttaa ttattttagat ttgttaacatt gaaattgggt
3301 ataa

FIG. 40B

ପାତ୍ରବିନ୍ଦୁ ୧୦୫

FIG. 41



ttta

attacccaactttgaggttagcattgctcttcaatcat atg gat tcg ttg ttt cag atg gca tcc gca
M D S L F Q M A S A

atg aag ttt caa tac tac tcg aag aaa gct gct gga aag aca atg tct aat agt gtc tcc
M K F Q Y Y S K K A A G K T M S N S V S

atg tcc agt gac aat cgc atg gag gat ttt aaa cgt cgt ttt cgt cga agt gga tcg tta
M S S D N R M E D F K R R F R R S G S L

gga att cca ttt gtc cca gaa gaa gat gtt aaa caa ctc ttc aca cca act cgt act gtt
G I P F V P E E D V K Q L F T P T R T V

cgt cga gaa gca tct att cgc gaa ggg gat gag gaa gaa gga gta caa att ctc aca ata
R R E A S I R E G D E E G V Q I L T I

att gtc aag tca agt cgt gtt tcg gag gat atc tca aaa atg att gca aac ctc cct gat
I V K S S R V S E D I S K M I A N L P D

cac act cgt atc aaa cat ttg gag act cgt gac agt caa gat gga agt tcc aaa act atg
H T R I K H L E T R D S Q D G S S K T M

gat gtt ctt cta gag att gag ctc ttt cat tat gga aaa caa gaa gca atg gat ctt atg
D V L L E I E L F H Y G K Q E A M D L M

aga ctt aat ggg ctt gat gtt cat gag gtg tca tcg act att cgt cca act gca ata aaa
R L N G L D V H E V S S T I R P T A I K

gag caa tat aca gag cct gga tct gat gat gcg aca acc ggt tct gaa tgg ttt cca aaa
E Q Y T E P G S D D A T T G S E W F P K

agt att tat gat ttg gat att tgt gca aaa aga gtg att atg tat gga gca ggg ctg gac
S I Y D L D I C A K R V I M Y G A G L D

gct gat cat cct ggt ttc aaa gat acc gag tat cgt caa cgt cga atg atg ttt gct gaa
A D H P G F K D T E Y R Q R R M M F A E

ctg gcg ctc aat tac aaa cac ggt gag cca att ccg cga acc gaa tat aca tca tcc gaa
L A L N Y K H G E P I P R T E Y T S S E

cgg aaa act tgg gga att ata tat aga aaa ttg aga gaa ttg cac aaa aag cac gca tgc
R K T W G I I Y R K L R E L H K K H A C

aag cag ttt ctt gat aac ttt gag cta ctg gag aga cat tgt gga tac tcg gaa aat aat
K Q F L D N F E L L E R H C G Y S E N N

att ccg caa cta gaa gat atc tgc aag ttt ttg aaa gca aaa act gga ttc cgt gtt cgc
I P Q L E D I C K F L K A K T G F R V R

FIG. 42

cca gtc gcc gga tac tta tca gct cgt gat ttc ttg gca ggt ctt gca tat cgt gtc ttc
P V A G Y L S A R D F L A G L A Y R V F

ttc tgc actcaa tac gtt cgc cat cat gcc gat cca ttt tac act cca gaa cca gac acc
F C T Q Y V R H H A D P F Y T P E P D T

gtt cac gag ctc atg ggt cac atg gct cta ttc gct gat cca gat ttt gct cag ttt tct
V H E L M G H M A L F A D P D F A Q F S

caa gag att gga tta gct tct ctt gga gca tca gag gaa gat ttg aag aag ctt gca aca
Q E I G L A S L G A S E E D L K K L A T

ctc tac ttc ttt tcc att gaa ttt ggt ctc tcg tct gat gac gct gcc gat tct cca gta
L Y F F S I E F G L S S D D A A D S P V

aaa gaa aat gga tca aat cat gaa aga ttt aaa gta tac gga gca gga ctt ctg agc agt
K E N G S N H E R F K V Y G A G L L S S

gct ggc gag ttg caa cat gcc gtt gag ggt agt gca acc att att cgt ttt gat ccg gat
A G E L Q H A V E G S A T I I R F D P D

cgt gtt gtt gag caa gaa tgt ctc att act act ttc cag tca gcg tat ttc tat act aga
R V V E Q E C L I T T F Q S A Y F Y T R

aat ttt gaa gag gcc cag cag aaa ctc aga atg ttc acc aac aac atg aaa cgt ccc ttc
N F E E A Q Q K L R M F T N N M K R P F

att gtt cgt tac aac cca tac aca gaa agc gtc gaa gtt ctc aac aac tcc cgt tcc att
I V R Y N P Y T E S V E V L N N S R S I

atg ttg gca gtg aac tct ctc cgc tca gac atc aac ctg ctc gcc gga gct ctc cac tac
M L A V N S L R S D I N L L A G A L H Y

atc ctg tag
I L *

FIG. 42

attacccaagttttaggttagcattgctctttcaatcat
atg gat tcg ttg ttt cag atg gca tcc gca atg aag ttt caa tac tac tcg aag aaa gct
M D S L F Q M A S A M K F Q Y Y S K K A
gct gga aag aca atg tct aat agt gtc aaa aac tgg att ccg tgt tcg ccc agt cgc cg
A G K T M S N S V K N W I P C S P S R R
ata ctt atc agc tcg tga ttt ctt ggc agg tct tgc ata tcg tgt ctt ctt ctg cac tca
I L I S S *
ata cgt tcg cca tca tgc cga tcc att tta cac tcc aga acc aga cac cgt tca cga gct
cat ggg tca cat ggc tct att cgc tga tcc aga ttt tgc tca gtt ttc tca aga gat tgg
att agc ttc tct tgg agc atc aga gga aga ttt gaa gaa gct tgc aac act cta ctt ctt
ttc cat tga att tgg tct ctc gtc tga tga cgc tgc cga ttc tcc agt aaa aga aaa tgg
atc aaa tca tga aag att taa agt ata cgg agc agg act tct gag cag tgc tgg cga gtt
gca aca tgc cgt tga ggg tag tgc aac cat tat tcg ttt tga tcc gga tcg tgt tgg tga
gca aga atg tct cat tac tac ttt cca gtc agc gta ttt cta tac tag aaa ttt tga aga
ggc cca gca gaa act cag aat gtt cac caa cat gaa acg tcc ctt cat tgt tcg tta
caa ccc ata cac aga aag cgt cga agt tct caa caa ctc ccg ttc cat tat gtt ggc agt
gaa ctc tct ccg ctc aga cat caa cct gct cgc cgg agc tct cca cta cat cct gta g

FIG. 43

FIG. 44A

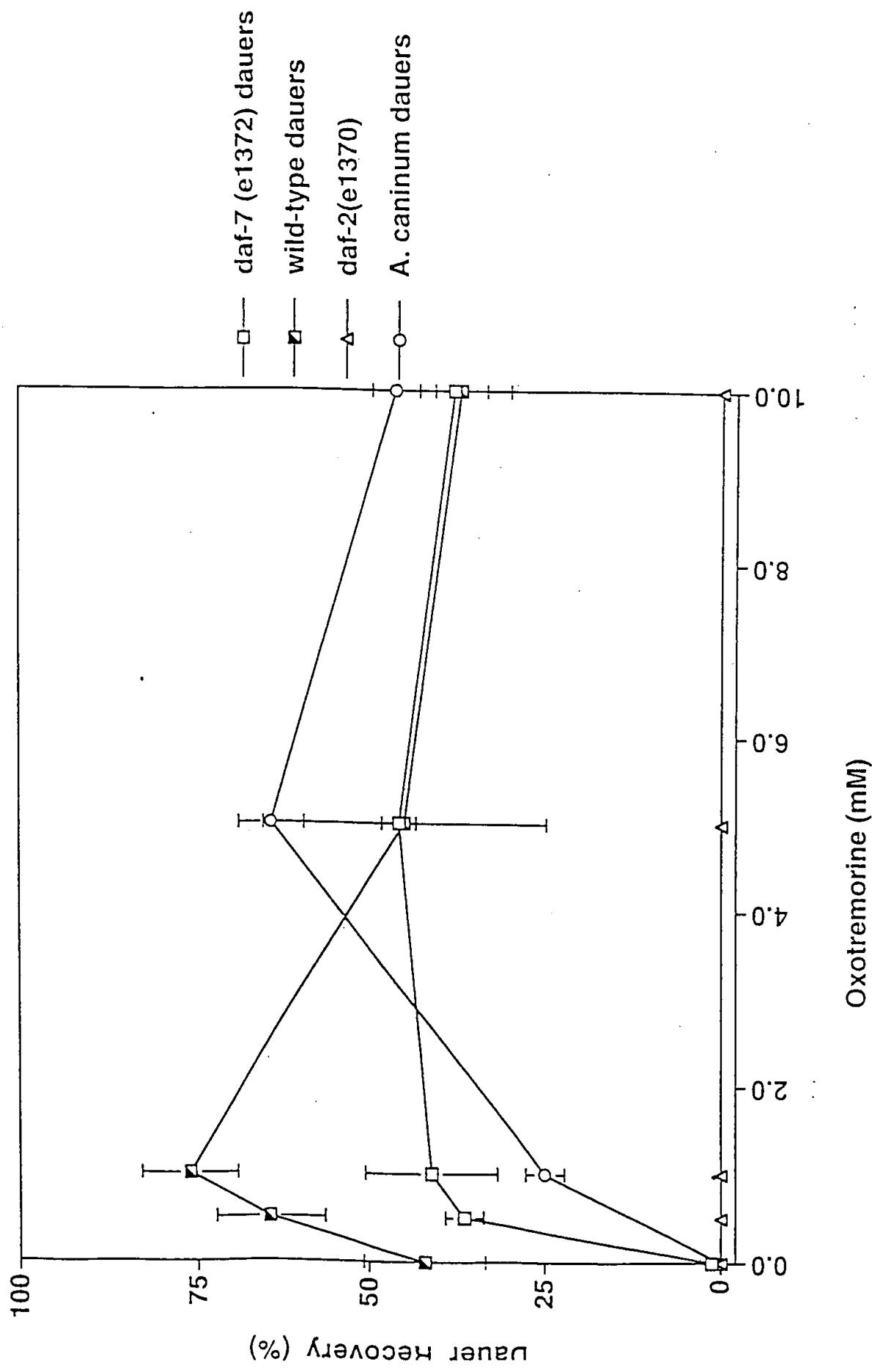


FIG. 44B

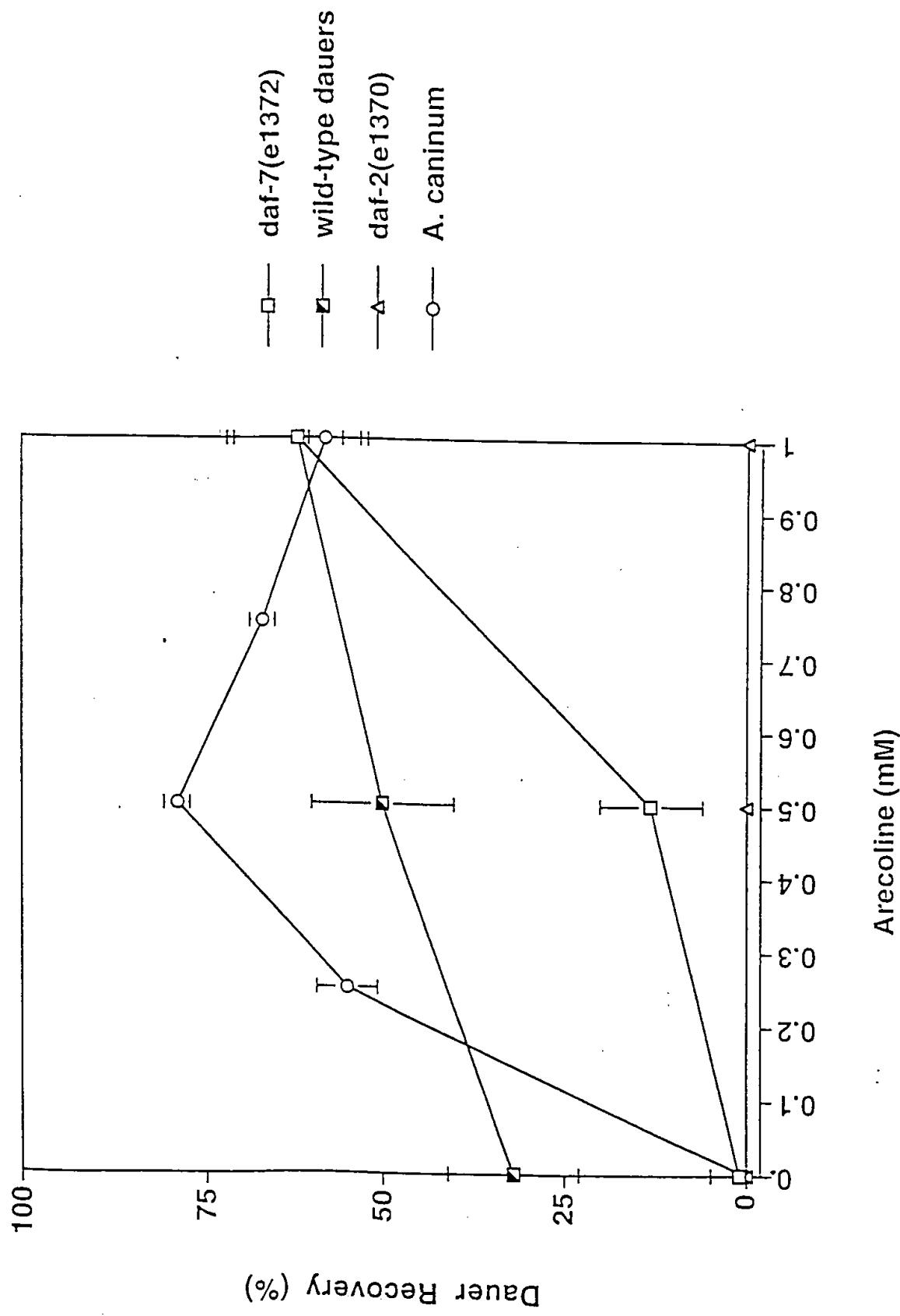


FIG. 45A

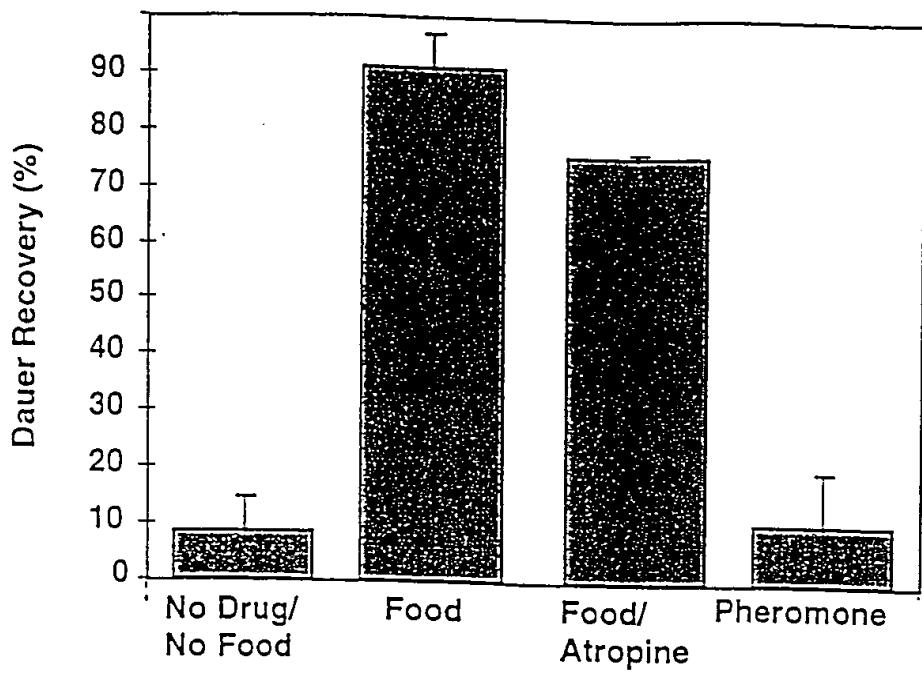


FIG. 45B

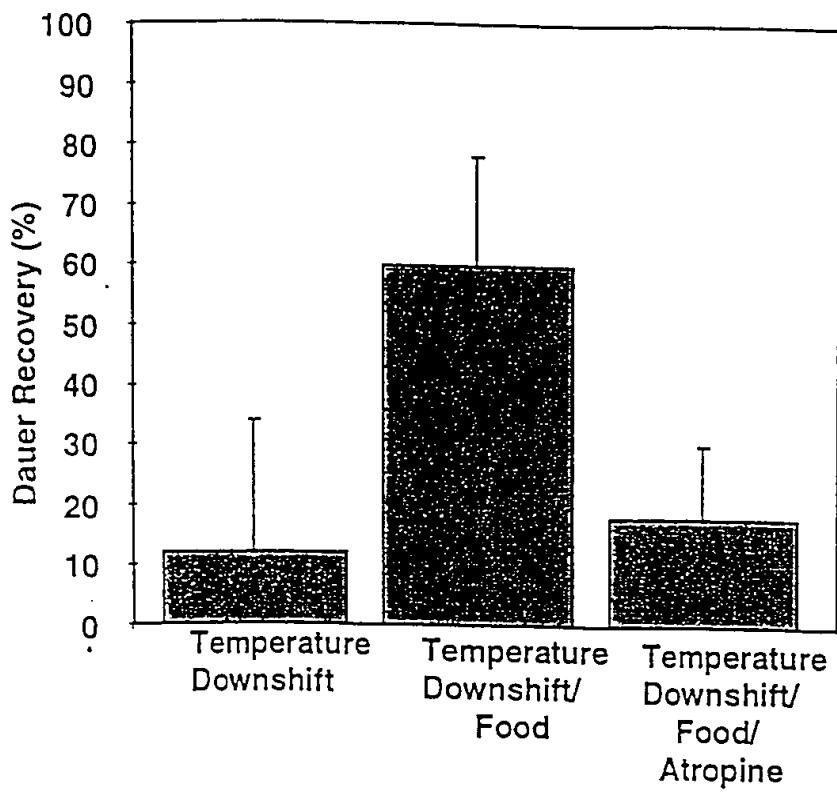
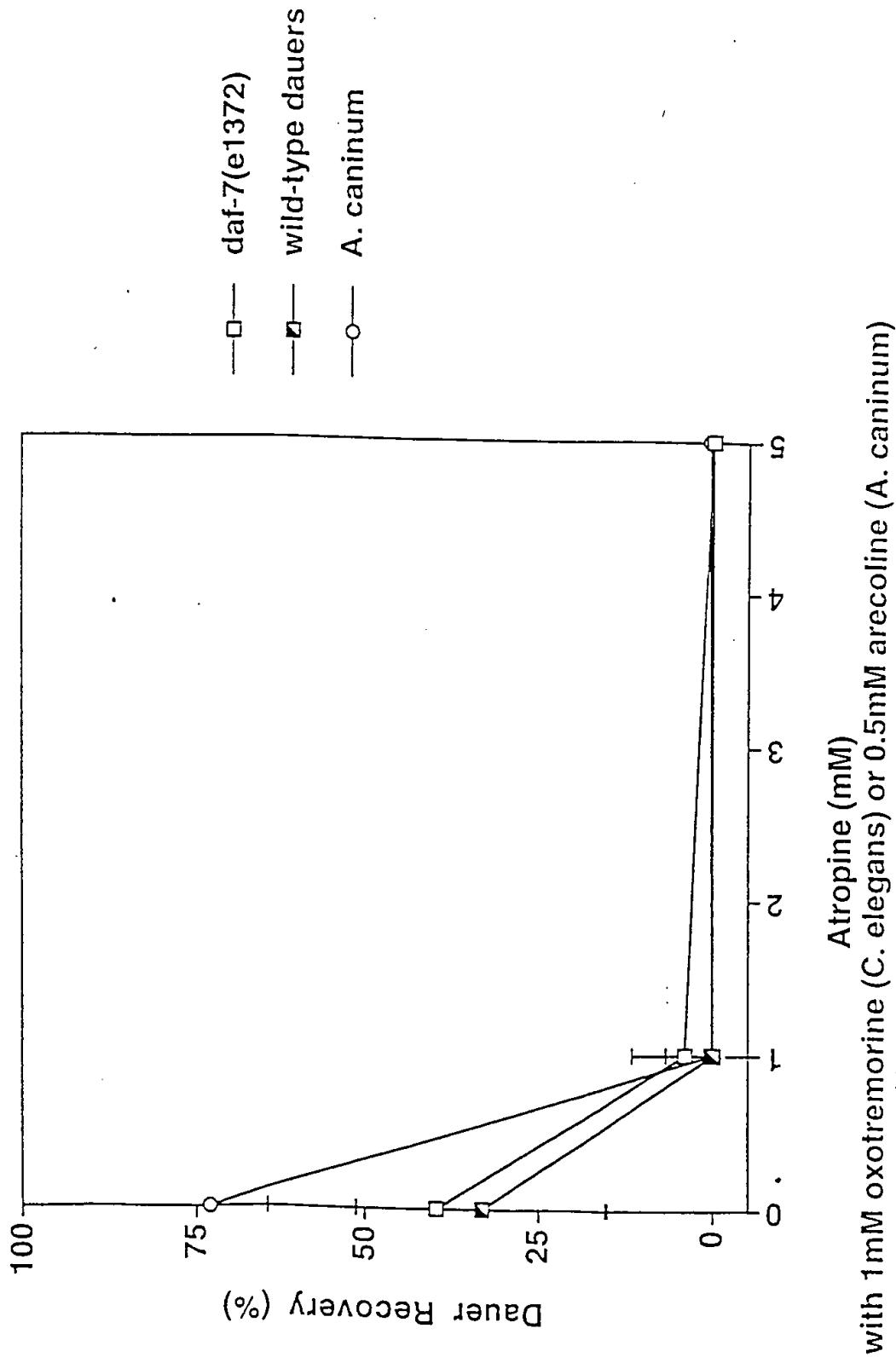
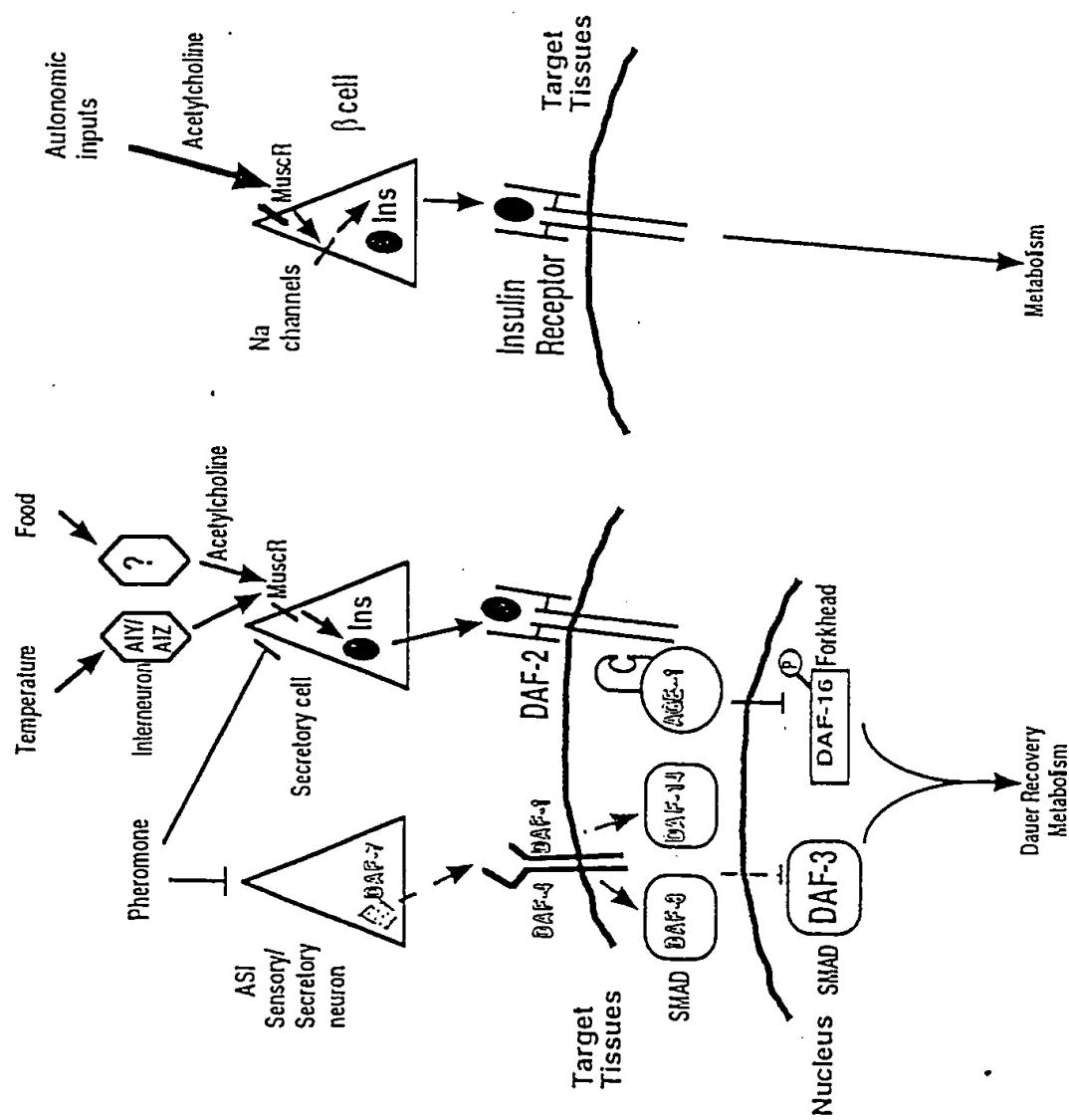


FIG. 44C



C. elegans



Mammals

ATTGGCATGAGCATGGaGCTTCGAGTCCTAGAGAACACAAAACGTTCCGGCGAACCTGGGtCTGGACTGCGAC
GAGACTCAAGCGAGTCCCGTGTGCCGATATCCCCTCACAGTGGACTTTGAGGCTTCGGCTGGACTGGATCAT
CGCACCTAACGCTACAAGGCCAACTACTGCTCCGGCCAGTGGGAGTACATGTTCATGCAAAATATCCGCATACC
CATTGGTGCAGCAGGCCAATCCAAGAGGTTATGcTGGCCCTGTTGATACCCCCACCAAGATGTCCCCAATcAAC
TgcTctACTTCAATGACAAGCAGCAGATTATcTACGGCAAGATCCCTGGCATGGTGGATCGCTGTGGcTGCTC
TTAAGGTGGGGATAGAGGATGCCTCCCCACAGACCGTACCCCAAGACCCATAGCCcTGCCCAATCCACCGCCTG
ATCCAAACAT

FIG. 47A

IRHEHGASSPREHKTTPAEPGGLRRDSSESRCCRYPLTVDFEAFGWDWIAPKRYKANYCSQWEYMFMQKYPHT
HLVQQANPRGYAGPCCTPTKMSPINMLYFNDKQQIIYGKIPPLAMVVDRCGCS

FIG. 47B